THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

MARCH, 1914

ORIGINAL ARTICLES

THE ETIOLOGY AND PATHOGENESIS OF BRONCHIECTASIS.

By C. P. Howard, M.D.,

PROFESSOR OF INTERNAL MEDICINE, UNIVERSITY OF IOWA, IOWA CITY, IOWA.

Since the young French student Cayol first called the attention of his preceptor, Laennec,[1] to a bronchiectatic lung, many theories have been advanced as to the etiology and pathogenesis of this interesting condition. Clinically it is rare, though relatively common in the autopsy room in association with phthisis, as is pointed out by Fowler.[2]

We are, therefore, rather fortunate in being able to report 4 cases which occurred among 967 medical admissions to the University Hospital: 3 of them were under twenty years of age and 1 over forty. In Lebert's series of 83 cases, 47 per cent. occurred before and 53 per cent. after the fortieth year, while in Acland's series of 60 the percentages were 77 and 23 respectively. The predominance of the male sex must be largely due to the greater number of male admissions to the general hospitals from which the majority of the reports are drawn.

Anatomical and clinical classifications have been advanced by almost every writer on the subject. The generally accepted anatomical one includes three groups: (1) A regular or cylindrical bronchiectasis, in which there is dilatation of the tubes toward the periphery of the lung, and (2) a fusiform type, in which, in addition

[1] De l'Auscultation Mediate, 1819, i, 124 (Brosason et Chaudé, Paris).

[2] Diseases of the Lungs, by J. K. Fowler and R. J. Godlee, 1898, 123 (Longmans, Green & Co., London).

to the above there is a dilatation at the periphery resulting in a bulbous termination; (3) the globular or sacculated type, in which the dilatations are strictly terminal.

Of the many clinical classifications, in our opinion that of Hoffmann[3] seems the most scientific. He recognizes four groups: (1) Inflammatory, (2) vicarious, (3) congenital, and (4) atelectatic.

1. The inflammatory group comprises the vast majority of the cases, and is nearly always of the saccular type. Two main subdivisions can be made: one associated with stenosis, and the other, the "indurative bronchiectasis," in which a thickened membrane attaches the portion of the lung affected with the ectasis firmly to the thoracic wall.

2. Vicarious or substituted type, in which the dilatation is always cylindrical. "When a portion of the lung has become inaccessible to the air and its volume is reduced, the traction excited on the adjoinging tissues during inspiration will cause them to make an attempt to fill the space." The powerful pull of the muscles which dilate the thorax and so act on the lungs will be unable to expand the impermeable portions, but will expand other ones. According to the position and circumstances, this may affect the alveoli or the bronchi, and thus arise vicarious emphysema and bronchiectasis; hence, the not infrequent association of the two conditions. The mucous membrane seems thinned like a serous membrane. No inflammatory processes take part in the disease; it is a true emphysema of the bronchi, but it has little or no importance clinically.

3. Congenital bronchiectasis was first described by Grawitz[4] and subsequently by Neisser.[5] Grawitz recognized three varieties: (*a*) A universal ectasia, in which there is a large common cavity with numerous recesses; (*b*) telangiectatic, in which only the smaller bronchi are attacked. These may be regarded as a malformation or as the result of some intra-uterine disease, as syphilis. The morbid process is usually confined to one lung, which may present a cyst with a central space branching into a peripheral set of intercommunicating secondary and teritary cysts, with serous contents. (*c*) Grawitz described a third variety, with numerous separate cysts formed on the bronchi of the third and fourth order, some communicating with the bronchial lumen and others closed. Goitre was found associated with this malformation. (*d*) Lastly, congenital bronchiectasis may be due to a dermoid growth invading a bronchus, as described by Cyril Ogle.[6] These congenital cases are comparatively rare, and have never been seen by the writer.

[3] Diseases of the Bronchi, Lungs, and Pleuræ, 1903, 178; Nothnagel's Practice (W. B. Saunders & Co., Philadelphia and London.) (Edited by J. H. Musser).

[4] Archiv f. Path. Anat., Berlin, 1880. lxxxii, 217.

[5] Zeit. f. klin. Med., 1901, xlii, 88.

[6] Trans. Path. Soc., London, 1897. xlviii, 1909.

4. Atelectatic: Ewart[7] also speaks of the atelectatic variety of Heller, in which there is an abnormal growth of the bronchial cartilages, together with remnants of the unexpanded non-pigmented fetal lung tissue, with epithelium of the pavement variety.

ETIOLOGY. Let us first consider Fowler's classification of the various conditions, which may be responsible for the development of bronchiectasis.

A. *Intrinsic*, that is, conditions acting directly through the bronchi.

1. *Acute and Chronic Bronchitis.* Bronchial catarrh is regarded by the majority of writers as the chief and earliest etiological factor. The special action of the catarrh consists in the mechanical plugging of the bronchioles. Juergensen[8] believes that long-standing bronchial catarrh may under certain conditions produce a growth of the interstitial connective-tissue of the lungs, which further favors the origin of bronchiectasis. In children the bronchiectasis may run a very acute course, and the finest bronchi may undergo dilatation, a condition termed bronchiolectasis. It has been fully described by Fowler, Walter Carr,[9] and others in England, but has received scant attention in America. The isolation of the bacillus influenzæ by Leichenstern and M. Beck of Europe, and by Lord[10] and Boggs[11] of this country, in a large proportion of cases of bronchiectasis suggests the important role played by influenzal bronchitis in the etiology of bronchiectasis.

2. *Bronchial Stenosis.* Bronchial stenosis may result from (*a*) gumma of the bronchi; (*b*) tuberculosis; (*c*) the pressure of an aneurysm or a tumor; (*d*) a foreign body.

(*a*) The role of syphilis in bronchiectasis and other pulmonary diseases has been much underestimated since the days of Laennec, according to Bouchut and Dujol.[12] They refer to 5 cases of bronchiectasis of Laurent and Guerin, in all of which the Wassermann reaction was positive, and give in detail one case of their own in which other syphilitic lesions co-existed. L. A. Conner,[13] in a critical review of syphilis of the trachea and bronchi, found among 56 autopsies dilatation of the trachea three times and dilatation of both bronchi in 9 cases. He asserts: "The surprising thing is not that they occasionally occurred but that they should have been found so infrequently. In not more than 20 per cent. of the cases of permanent stenosis did bronchiectasis occur." It seems evident, therefore, that the tracheal or bronchial stenosis is not the chief determining cause of the bronchiectasis found. "Much more potent

[7] Allbutt and Rolleston's System of Medicine, 1909, v, 127 (McMillan & Co.)

[8] Handbuch der speciellen Pathol. u. Therap., 1877, H. Ziemsen, Band v, i, 286 (Liepsig, F. C. W. Vogel).

[9] Practitioner, 1891, xlvi, 87.

[10] Boston Med. and Surg. Jour., 1902, cxlvii, 662, ibid., 1905, cliii, 537 and 574.

[11] AMER. JOUR. MED. SCI., 1905, cxxx, 902.

[12] Rev. de Med., 1912, xxxiii, 585.

[13] AMER. JOUR. MED. SCI., 1903, cxxvi, 57.

factors are the changes occurring in the bronchial wall and in the adjacent lung tissue, by which the muscular and elastic tissue of the bronchi upon which their strength and resilience depend is replaced by inflammatory tissue." Osler and Gibson[14] speak of three pathological types of syphilitic bronchiectasis: (1) With an interstitial pneumonia of the lower lobes, adherence of the pleura with general dilatation of the bronchi and cavity formation; (2) cases with a large single cavity in the upper lobe, with smooth thick walls; (3) cases which follow stenosis of the bronchus. In children certain cases run an acute course and reveal at autopsy a picture identical with that described by Grawitz as congenital bronchiectasis. While the "honey-comb" appearance of a bronchiectatic process limited to one lobe is usually due to syphilis, Weill and Gardere[15] have recently reported two cases in children of three and ten years respectively in which the honey-comb lung was due to tuberculosis. The important conclusion to be drawn from the above observations is that syphilis plays an important role in the etiology of bronchiectasis and should always be excluded in a given case.

(*b*) Tuberculosis: Tuberculous processes are so slow that the lung can accommodate itself to the altered conditions, though stenosis may occur as the result of erosion through the bronchial wall. Chevelier Jackson[16] has seen 6 cases illustrating this possibility. The following case belongs in all probability to this category.

CASE I.—Pulmonary tuberculosis (?); bronchial stenosis; bronchiectasis. M. D., aged forty-five years; laborer. Admitted March 13, 1913. Not referred. Clinical No. 881. Complaints: "Spells of coughing."

The family history was negative for tuberculosis. Patient was a day laborer, and had worked much recently in dusty atmospheres, shovelling coal. He had used alcohol to excess for years. He admitted gonorrhea at thirty-two years, at which time he had a single sore on the penis, for which he took local treatment and one bottle of medicine, and never developed any secondaries. He denied absolutely ever having been sick in bed in the past twenty years, but finally admitted to having some cough, with slight amount of sputum, for the past ten or fifteen years. Ten years before the onset of the present illness he had a pleurisy of the left side, which lasted for a day or two. In October, 1912, during a paroxysm of coughing, something "seemed to break" in his chest, and the sputum for a day or so following was especially offensive.

The present illness dated from January 17, 1913, when, following

[14] System of Syphilis (Edited by D'Arcy Power and J. Keogh Murphy), 1909, III, vii, (London-Oxford Med. Pub.).

[15] Lyon Méd., 1912, cxviii, 1221.

[16] Jour. Amer. Med. Assoc., 1912, lix, 1123.

a prolonged spree, he developed cough and sputum. The cough was paroxysmal in character, associated with change of posture, and was especially frequent in the early morning. The sputum was profuse, and was so offensive as to be noticed by his fellow-workmen. It was usually yellowish in character, but occasionally had been blood-streaked. Since the present onset the patient had had chills, fever, and night sweats, and, though not confined to bed, he had not been at work. The appetite had been good. He fell from an average weight of 155 pounds to 133 pounds.

Physical examination revealed a well-developed and fairly well-nourished man, with flushed face, due in part to cyanosis and in part to dilatation of the venules. There was also cyanosis of the ears, lips, and finger tips, but no clubbing, though slight incurvature of the nails. The breath was extremely offensive, and of the same odor as the sputum. The thorax was of the emphysematous type, with somewhat restricted expansion, but no apparent flattening or retraction. Litten's sign was present on both sides. The percussion note was hyperresonant, except in the lower left interscapular region and base, where it was distinctly dull. Over this area vocal fremitus was diminished, and the breath sounds enfeebled and accompanied by numerous medium moist rales and high piping sonorous and sibilant rales. The heart revealed a normal area of dulness without displacement. The sounds were loud, regular, and clear, and there was no special accentuation of either second sound. Pulse was 84, large, full, and regular in force and rhythm. Blood pressure, 108 mm. (Faught); vessel wall distinctly palpable. The abdomen was round and soft. The liver was pushed somewhat downward by the emphysematous lungs, so that the relative cardiac dulness reached 5 cm. below the costal border in the right parasternal line. The edge of the spleen could not be felt. Hemoglobin, 70 per cent. (Sahli); red cells, 4,700,000; white cells, 16,600. Differential count: Polynuclears, 81 per cent.; lymphocytes, 15 per cent.; large mononuclears, 3 per cent.; transitionals, 1 per cent. Wassermann test was negative on two occasions. Von Pirquet test was positive. The urine contained very slight traces of albumin and an occasional hyaline and granular cast. The sputum varied from 165 to 300 c.c. in amount, and was yellow, purulent, separating into three layers, and having a distinctly sweetish, offensive odor; on one or two occasions it contained elastic tissue; repeated examinations, however, failed to reveal acid-fast bacilli. Cultures were negative for Bacillus influenzæ, but numerous staphylococci and streptococci could be isolated. The skiagram revealed in the lower left back a distinct shadow corresponding to the area of impairment (Fig. 1). There was no evidence of infiltration of either apex. The patient on admission was running a high, irregular fever, which persisted for some two or three weeks, and was associated with a progressive loss in weight. Hypodermic injections of guaiacol

cleared up the offensive odor of the sputum, and the daily inhalations of creosote also for a time caused considerable improvement in the patient's well-being, though the amount of sputum remained excessive.

On April 23, on account of another exacerbation of fever, sweats and chills, and increase in the area of dulness, an aspirating needle was introduced into the eighth left interspace in the scapular line. After considerable resistance was overcome the needle was steadily introduced into the lung substance, and though nothing could be aspirated into the Ricord syringe, after withdrawal of the needle

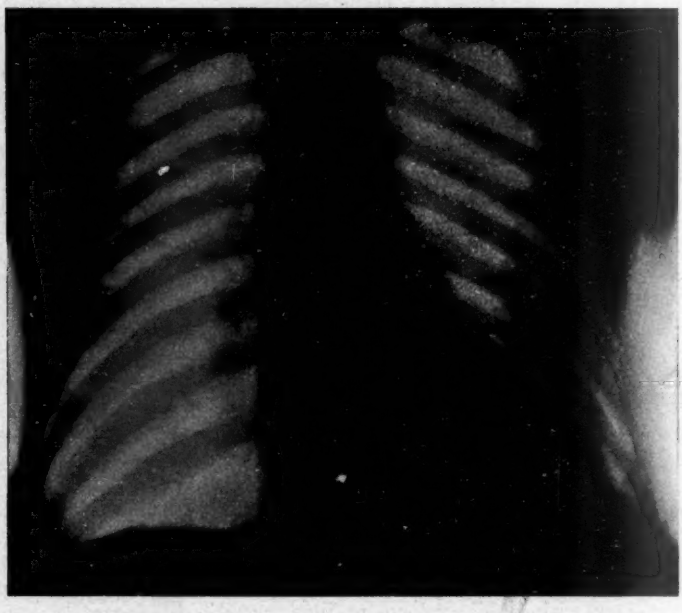


FIG. 1.—Case I. Pulmonary tuberculosis; bronchial stenosis; bronchiectasis.

a small particle of thick, yellowish pus was found in the needle, which, in smears, showed numbers of pus cells and many bacteria, diplococci, and small bacilli. On April 26 a second puncture in the ninth interspace closer to the vertebral line was performed, but with absolutely negative results, though on this occasion a needle with a still larger lumen was used. Another skiagram revealed a more definite shadow corresponding to the increased area of dulness.

Under local anesthesia, on May 2, Dr. L. W. Dean introduced a bronchoscope into the left bronchus. This revealed, fourteen

and a half inches from the upper central incisor teeth, red granulation tissue and a cicatricial stenosis, which after some difficulty was eventually dilated, resulting in the evacuation of two ounces of foul, thick pus. The cavity was thoroughly cleansed, with cocaine and adrenalin, and the walls carefully examined. The latter were covered with red granulations, but no trace of a foreign body could be found. The drainage afforded by this procedure was followed by a temporary improvement in the patient's condition. Before subsequent dilatation could be carried out the patient left the hospital without permission.

(*c*) Many cases of thoracic aneurysm or mediastinal tumor exerting sufficient pressure on a main bronchus to bring about a certain degree of stenosis have been observed. In some of these cases bronchiectasis may result, as was frequently observed by Osler, who has termed it "aneurysmal phthisis."

(*d*) *Foreign Bodies.* The presence of a foreign body with partial obstruction of the bronchial lumen is not an infrequent cause. Cohn[17] found experimentally that dilatation usually occurs around the foreign body and not behind it. It is the continual irritation that causes the inflammation and ulceration and leads to a cavity formation. The local irritant acting continuously causes a peribronchitis which, extending from the site of the foreign body to the bronchi, favors in a special way the formation of bronchiectasis. Hoffmann states: "I must add that foreign bodies are too little considered as causes of bronchiectosis. We have cases enough in which the course and all the circumstances did not suggest the idea that a foreign body could have passed into the lungs and where the autopsy first showed to the astonishment of the physicians and friends what was the trouble; or the accidental expectoration of the foreign body established the diagnosis." Hoffmann believes that the stenotic form of bronchiectasis is of frequent occurrence, being present in many cases in which it is not recognized. Chevalier Jackson urges the importance of considering each case of bronchiectasis as a possible foreign body one. "Of course, it is not known how frequently foreign bodies may be the cause of the bronchiectasis, but the similarity of the symptoms in bronchiectasis and in foreign bodies in the bronchi would certainly render exploratory bronchoscopy advisable even in a case with negative radiograph." The importance of this warning has recently come home to me as the following case report will testify.

CASE II.—Foreign body; bronchial stenosis; bronchiectasis. W. D., aged seven years; schoolboy. Referred by Dr. Mighell, Marshalltown, Iowa. September 25, 1911. Clinical No. 336. Complaints: "Cough and vomiting."

Family History. The family history was negative for tuberculosis.

[17] Abhandl. d. Schles. Gesselsch. f. Vaterl. Kult. Phil. Hist. Abth. (Breslau), 1862, Heft i, 72.

Personal History. At the age of three he had lobar pneumonia, at five pertussis, and at six measles. Since the latter the patient had never been quite well.

Present illness began in February, 1911, with a severe cough occurring in paroxysms and associated with "vomiting up" of large amounts of yellow very offensive sputum. This might occur at any time during the day upon exertion or crying, but was more frequent and most abundant in the early morning. It was at times blood-streaked. The mother had noticed that the fingers were becoming short and stubby and that he was losing weight. A diagnosis of pulmonary tuberculosis was made by various physicians, and the sputum was examined repeatedly for tubercle bacilli, but with negative results. He first reported to the University Hospital in August, 1911, when he was examined by my associate, Dr. Van Epps, and a diagnosis of bronchiectasis made.

Physical examination on September 25 revealed a rather poorly nourished undersized boy weighing forty-one pounds. Face was pale. Definite clubbing of the terminal phalanges of both hands. The thorax was well-formed and symmetrical, but the right side moved less freely than the left. There was an area of definite dulness in the lower right back extending from the sixth dorsal spine to the base and from the posterior axillary fold to the spine. Over this area the breath sounds were amphoric and accompanied by numerous coarse moist rales. The left lung was clear on percussion, but revealed a few fine moist rales over the lower back. The heart showed no evidence of displacement or hypertrophy and the sounds were clear and of relative normal intensity. The pulse was 120, regular in force and rhythm, and of moderate volume. The abdomen was negative. On a subsequent examination the breath sounds over the dull area were suppressed, and it was noticed that these varied with the recentness of the paroxysm of the cough and expectoration. Hemoglobin, 60 per cent. (Sahli); red cells, 4,400,000, white cells, 21,000. The sputum was excessive, varying from 100 to 300 c.c. in the twenty-four hours; it was purulent, greenish in color, and settled into the characteristic three layers, and had an offensive odor. Microscopically on numerous examinations there were neither elastic tissue nor acid-fast bacilli, but great numbers of pus cells and diplococci, and occasionally some blood cells. A skiagram (Fig. 2) revealed a dense shadow corresponding to the dull area at the right base and merging with the right border of the heart.

He was given daily intratracheal injections of iodoform, with gradual amelioration in the amount of sputum and in the severity of the cough. During the last week of his stay in the hospital the amount varied between 20 and 140 c.c. in the twenty-four hours. As a precautionary measure, a day or two before discharge, an aspirating needle was introduced into the right pleura and into

the right lung, but no pus could be obtained. He was discharged on November 18, 1911, having gained six pounds in weight, and looking and feeling much better.

On December 12, 1912, Dr. R. F. French, of Marshalltown, Iowa, reported that the patient, during a fit of coughing, had brought up a tack which he remembered having swallowed in June, 1910, but which neither mother nor patient had thought of from that time. Upon receipt of this letter we immediately reëxamined the skiagram and found that we had overlooked the definite shadow of the tack lying head downward in one of the large bronchi of the right side. Dr. G. E. Hermence, who subsequently had charge of the patient, elicited the following new facts from the

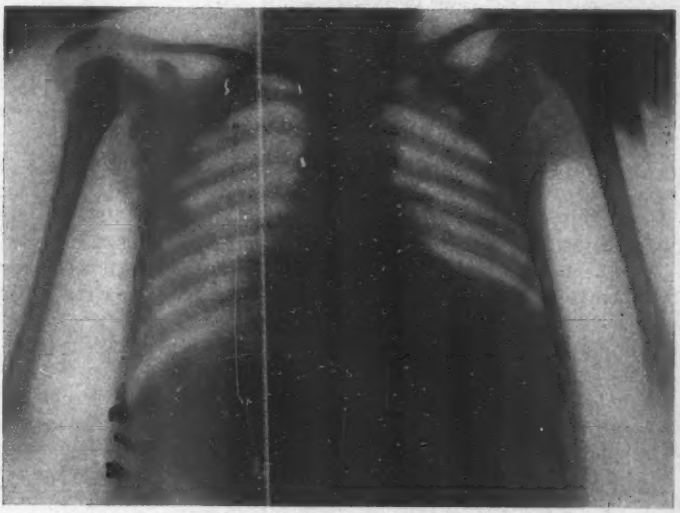


FIG. 2.—Case II. Foreign body; stenosis; bronchiectasis.

mother: She now remembered that the boy had swallowed the tack in June, 1910. At the time he had had a hard coughing spell, but recovered and the tack was forgotten. In January, 1911, he began to cough, especially in the morning, and it was noticed that he raised a large amount of sputum and had distinct fever, as high as 104° on one occasion. Since his discharge from the University Hospital the intratracheal injections were continued until September, 1912, when they were stopped on account of local irritation of the throat. About September 1, he was worse again, and in one of the paroxysms something seemed to "break in his side," which was followed by an unusually large amount of yellowish purulent material. In another violent paroxysm, on December 3,

something seemed to choke him, and upon putting his finger into the pharynx he pulled out the tack (Fig. 3). Since then the patient has felt better. The cough and sputum have gradually become less. A request for him to return to the hospital for examination was not granted, but Dr. Hermence, under date of April 24, 1913, reported that the cough and sputum have much lessened and that the latter has little or no odor. He had gained in weight, and now leads the normal life of a boy of his age. The physical examination still reveals an area of dulness at the original site.

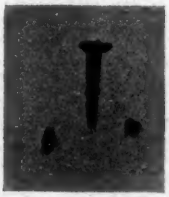


FIG. 3.—Tack expelled from bronchus by Case II. Note slight erosion of the head of shaft.

Hoffmann calls attention to the probable frequent origin of bronchiectasis from inhalation of solid particles. It is of interest to note that Case I of our series assigned the recent exacerbation of the cough and expectoration to the inhalation of coal particles while working in a railroad coal chute.

The importance of bronchial stenosis in the etiology of bronchiectasis has been demonstrated experimentally by W. G. MacCallum[18] and his pupils W. L. Thorton and J. P. Pratt.[19] Bronchial stenosis was produced either by a screw clamp around a bronchus or by placing short pieces of tubes, with different sized lumens, inside of the bronchus. When one bronchus was partially occluded the pressure changes in the lung behind the occlusion were marked; the greater the occlusion the greater the negative pressure on inspiration, and the greater the positive pressure on expiration. In addition, inspiration and expiration were so protracted that the opportunity for a pause no longer existed, and they occupied the whole cycle. When the lumen of a bronchus was reduced the lung corresponding to the bronchus involved failed to contract during expiration as completely as the lung with an unobstructed bronchus. Owing to this failure to completely contract an excess of air remained in the lung, which was consequently continually distended. What has been represented in these experiments as taking place rapidly must appear gradually in man as the result of a bronchial stenosis, due to the pressure of a tumor or some similar cause. If a foreign body be lodged in a bronchus the above changes

[18] Bull. Johns Hopkins Hospital, 1908, xix, 215. [19] Ibid., 1908, xix, 230

must follow very rapidly. "The partial occlusion of a bronchus causes air to be entrapped and the bronchus to be distended, with greater changes in pressure behind the obstruction during respiration. In coughing and related processes the pressure inside the bronchus is greater than the pressure outside the bronchus only by the force of the elastic recoil of the lung; so there is no marked tendency on the part of the bronchi to undergo dilatation."

3. *Bronchial Obstruction.* According to Lichtheim[20] sudden and complete obstruction of a bronchus causes in twenty-four hours collapse of the lung area to which it is distributed with purulent accumulation within the tubes. This is followed by emphysema of the surrounding tissue and in several weeks by dilatation of the neighboring bronchus. Occlusion of the bronchus does not necessarily cause a bronchiectasis in the area of supply unless there is also an opportunity for the development of a purulent bronchitis; hence a stenosis is more favorable for its development than an absolute occlusion. This was well illustrated in a case reported by Sutherland,[21] in which the bronchial obstruction was due to the impaction of an O'Dwyer tube; at the autopsy the greater part of the lower lobe was destroyed by an abscess and the remaining portion was collapsed and airless; the surrounding smaller bronchi were dilated and embedded in soft friable lung tissue.

B. *Extrinsic*, that is, conditions acting indirectly through disease of the lungs or pleuræ.

1. *Pulmonary Changes.* (*a*) *Collapse of the Lung.* This exciting cause is common in the child as a result of capillary bronchitis or of bronchial stenosis, as has already been described.

(*b*) *Pneumonia.* Either the lobar or lobular variety is regarded by many as a common cause. It must be borne in mind that lobular pneumonia also frequently supervenes in a well-established bronchiectasis. (Compare Case III.)

(*c*) *Emphysema.* A moderate degree of bronchiectasis is usually found associated with old-standing cases of emphysema.

(*d*) *Fibrosis of the Lung.* Fibrosis of the lung, sometimes termed cirrhosis of the lung, may result from an unresolved or chronic pneumonia or from the fibrosis developing in certain cases of pulmonary tuberculosis. Ewart emphatically states that bronchiectasis (Rokitansky to the contrary) may occur in subjects of chronic phthisis; on the other hand, chronic bronchiectasis may end in tuberculosis, though this is a rare event.

Hoffmann believes a tuberculosis establishing itself in the finer branches of the bronchi may lead to the formation of small bronchiectatic areas, which, however, do not produce clinical symptoms and are therefore not named in the clinical account of bronchi-

[20] Archiv f. experimentelle Pathologie u. Pharmakologie, 1879, x, 54.
[21] Lancet, 1892, i, 189.

ectasis. In many cases of so-called fibrous phthisis characteristic bronchiectasis occurs, and their course will indicate that the cicatricial contraction of the tissue was really the cause of the bronchial dilatation.

Syphilis in the form of bronchial gummas has already been referred to, but it must be mentioned that specific scar formation and infiltration of the parenchyma are especailly favorable for the production of bronchiectasis.

2. *Pleural Changes.* Pleurisy with effusion, whether serous or purulent, will result in collaps of the lung; dilatation of the bronchi and chronic thickening of the interlobular and interalveolar connective-tissue may follow in the order named, or these changes may proceed together. Extensive pleuritic thickening at the base cripples the lung and the respiratory function may be entirely lost.

In a given case it is difficult if not impossible to state which one of these various extrinsic factors is responsible for the bronchiectasis. In fact they may all be present in any one case, and it is perhaps best to group those cases under the general term of "pleuropneumonic." The following histories are illustrative:

CASE III.—Pleuropneumonic bronchiectasis. A. C., aged fourteen years; schoolgirl; white; American. Clinical No. 405. Admitted September 17, 1910. Referred by Dr. Post of Maquoketa. Complaints: "Cough and profuse expectoration."

Family History. Negative for tuberculosis or other lung trouble.

Personal History. Had chickenpox and measles in early childhood. In 1903 she received an injury (?) to the back, from which she was confined to bed on account of pain, cough, and high fever.

Present illness began in December, 1907, with an attack of scarlet fever, complicated by severe pain in the left side. It was not known whether the patient had a pneumonia or a pleurisy at that time. For two years subsequently she suffered from a troublesome cough, but without sputum. About September, 1909, expectoration made its appearance. It was profuse, yellowish in color, and with an offensive odor, and at times blood-streaked. The cough became paroxysmal, occurring at intervals during the day, but more particularly in the morning. She averaged about five or six attacks in the twenty-four hours. She did not notice any effect of posture. At times the sputum would fill a teacup. During the last two or three years the mother had noticed gradual enlargement of the finger tips, and a liability to chills, fever, and sweating. The patient had lost ten to twelve pounds in weight. There had been slight cyanosis.

Physical examination showed that the patient was still well-developed and nourished. Weight, eighty-four pounds. The finger tips were markedly clubbed and the nails incurved; there was also slight clubbing of the big toes, with incurvature of the nails, but no enlargement of the bones. The thorax was decidedly long and

narrow, with a somewhat acute costal angle. The left upper front was flatter and moved less with respiration. The right lung was resonant, and except for somewhat harsh breath sounds in the second and third right interspaces and a few medium moist rales over the back, was normal throughout. The left lung revealed an area of dulness beginning at the level of the fourth dorsal spine and extending to the base and outward to the midscapular line. Over

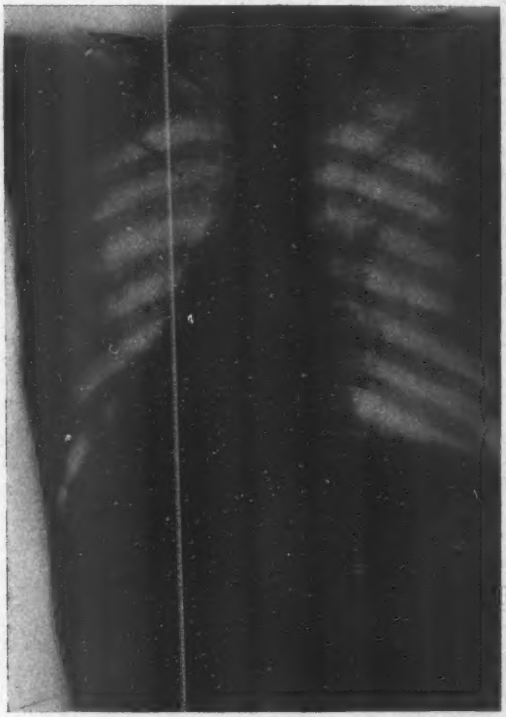


FIG. 4.—Case III. Pleuropneumonic bronchiectasis.

this dull area the breath sounds were enfeebled, except after a paroxysm of coughing, when they became distinctly bronchial, and almost amphoric in character. Everywhere throughout the left lung, but particularly over the lower lobe, were heard numerous medium and large moist rales. There was no displacement of the heart, no evident enlargement of the right chamber, and no abnormality of the heart sounds. The sputum varied in amount from 410 to 200 c.c. in the twenty-four hours. It presented the charac-

teristic three layers, had a greenish-yellow color and a fetid, sweetish odor. It contained many pus cells, but daily examination failed to show the presence of elastic tissue or tubercle bacilli. The blood count on September 22 revealed hemoglobin, 80 per cent. (Tallquist); red blood cells, 5,060,000; white blood cells, 12,000. Differential count: Polynuclears, 75 per cent.; lymphocytes, 14 per cent.; large mononuclears, 10 per cent.; eosinophiles, 1 per cent. The von Pirquet test was negative on two occasions. The skiagram (Fig. 4) on September 17 revealed enlarged glands in the hilum of the right lung. On the left side below the cardiac shadow there was an abnormal opacity, 10 cm. in diameter, corresponding in position to the signs of the cavity on physical examination. On September 27 she was started on the intratracheal injections of iodoform. In addition she received general dietetic and hygienic supervision. With the exception of a sudden onset of chill, fever, pain in the left side, and the presence of a dry friction rub, due to an infection of the left pleura on October 24, 1910, and again on January 17, February 25, and February 28, 1911, the patient gradually and progressively gained in strength and weight, and the amount of sputum fell to about 75 to 100 c.c. in the twenty-four hours. On February 28 the patient coughed up 270 c.c. of fetid sputum, which suggested a temporary obstruction to the outflow of the cavity, though on this as on previous occasions a friction rub was audible. On March 14, 1911, the white blood cells were 8000, and the polynuclears 88 per cent. On March 21 the patient was discharged, having gained twenty-four pounds in weight, and having only one or two paroxysms in the twenty-four hours. The sputum on the last day measured 60 c.c. The signs at the left base, however, remained unaltered. In the hope of finding a definite abscess cavity and draining the same by surgical means, an aspirating needle was introduced into the ninth interspace in the back corresponding to the middle of the dull area, but no pus could be obtained.

A letter from the mother on March 25, 1913, reported that the patient weighed 125 pounds, which meant an additional gain of fourteen pounds since discharge. The cough and sputum, however, persisted.

CASE IV.—Pleuropneumonic bronchiectasis. C. M., male, aged seventeen years; schoolboy. Referred by Dr. W. H. Spencer, of Cedar Rapids. Admitted October 27, 1910. Clinical No. 83. Complaints: "Stomach trouble." Father and mother, four brothers, and three sisters living and well. Tuberculosis on both paternal and maternal sides of family.

Personal History. Patient was born and bred in Iowa. He had measles and whooping cough in childhood, but denied pneumonia and pleurisy previous to the present illness. The mother stated that he had been subject to winter cough since his eleventh or

twelfth year, associated with sputum. Average weight at fifteen years was 115 pounds.

The present illness dated from his fourteenth year, when he had an "abscess in the left side," since which he had never been strong. For the last three years he had practically a constant cough, associated with the expectoration of large amounts of greenish-yellow and offensive sputum, especially profuse in the early morning. At fifteen years he had several attacks of hemoptysis. He had dyspnea on exertion and fever until six months before admission. The appetite became poor, and he had lost steadily in weight. The sputum had been repeatedly examined for tubercle bacilli, but with negative results.

Physical examination revealed a tall, slim, delicate-looking youth of blond complexion. Weight, 107 pounds. There was dyspnea on the slight exertion of undressing. He was a mouth breather. There was definite clubbing of the finger tips and well-marked incurvature of the nails, with slight cyanosis of the nail beds. The thorax was large, well-developed, and slightly asymmetrical in front, the left side being smaller than the right and expanding less. The left back seemed flatter than the right. The percussion note was everywhere resonant except in the lower left back, where it was impaired, though not actually dull. Over the impaired area tactile fremitus and vocal resonance were somewhat increased, while the breath sounds had a distant blowing, almost tubular quality. Over the entire left back there were numerous medium moist rales, with here and there a fine crepitant rale. The right lung was resonant throughout, while the breath sounds were vesicular except in the lower right axilla and right back from the angle of the scapula to the base, where they were distinctly harsh and accompanied by numerous medium moist rales and bronchophony. The heart was neither hypertrophied nor displaced. The heart sounds were clear at the apex, while at the base the pulmonic second sound was distinctly accentuated. The pulse varied from 90 to 112 to the minute, regular, of fair volume, and moderate tension. The abdomen was flat and soft, and neither liver nor spleen was palpable. The blood revealed hemoglobin, 53 per cent. (Sahli); red blood cells, 5,250,000; white blood cells, 15,600. Differential count: Polynuclears, 73 per cent.; lymphocytes, 24 per cent.; large mononuclears, 3 per cent. The urine was normal. The sputum varied in amount from 150 to 190 c.c. in the twenty-four hours, and had a distinctly sweetish odor at times, but at others was offensive. Microscopically it was negative for acid-fast bacilli and elastic tissue on seven observations. The von Pirquet test proved negative. Temperature ranged between $98\frac{1}{5}°$ and $99\frac{4}{5}°$. On October 27, 1910, a skiagram (Fig. 5) revealed a distinct shadow at the left base, merging with the heart dulness. There was also a slight increase in the normal shadow at the right hilum and a little opacity at

the right base. The patient received a few intratracheal injections, after which he went home with directions to his physician to continue treatment. He was lost sight of, and a letter from Dr. Spencer on April 14, 1913, reported that he had died some two years after his discharge from the hospital.

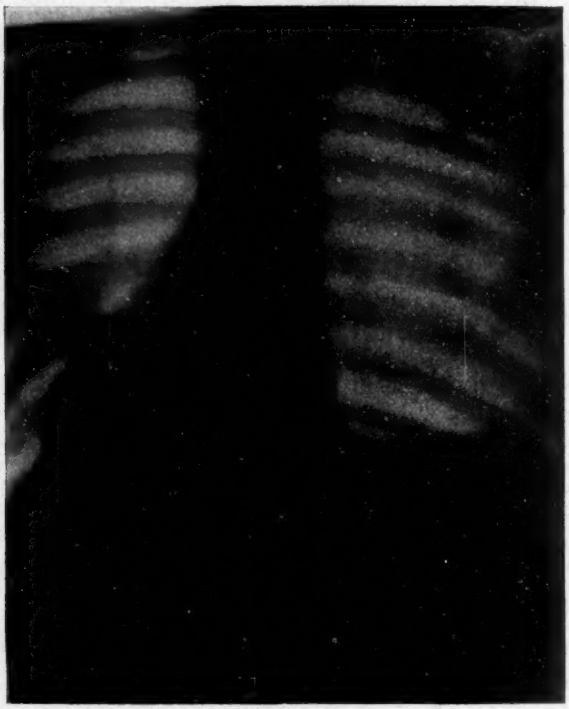


FIG. 5.—Case IV. Pleuropneumonic bronchiectasis.

PATHOGENESIS. The best *resume* of the various theories of the production of bronchiectasis is given by T. Grainger Stewart and G. A. Gibson,[22] and will be adopted in this paper with some modifications and additions.

1. The mechanical pressure of the stagnating secretion was first suggested by Laennec and adopted by other French pathologists. According to this theory the accumulation of the mucus, aided to a certain extent by cough, causes the dilatation. But there is no special accumulation of mucus in some cases, and further,

[22] Twentieth Century Practice of Medicine, 1896, vi, 552 (New York, Wm. Wood & Co.).

it is mechanically impossible when one considers the consistency of the secretion and the free outlet in two directions.

2. Concentrated air pressure is advocated by Reynaud, Williams, and others. The dilatation is explained as compensatory to atrophy or collapse of neighboring areas of the lung. Further, the pressure of the inspired air acts with greater force on the diminished respiratory surface. Against this theory are two facts: (1) Bronchiectasis arises without preëxisting cough, and cough is common while bronchiectasis is rare; (2) even if such a cause were present, emphysema rather than bronchial dilatation would result, for the bronchi are less yielding than the pulmonary tissue.

3. Extrabronchial traction was emphasized by Corrigan, Barth, and Hamilton. According to them dilatation resulted from traction upon the bronchial walls by the contracting cirrhous lung tissue aided by pleuritic adhesions to the chest wall. Against this speak the following facts: (*a*) Bronchiectasis often occurs without cirrrhosis and without pleural adhesions; (*b*) the possibility to demonstrate that the dilatation may precede in some cases the condensation of the lung; (*c*) the process of traction could never explain the opening of the dilatations into one another nor the formation of bridges in the dilated portions; (*d*) cirrhosis of the lung does occur without bronchiectasis, the latter being present in only 30 per cent. of the former according to Bastian.

4. Inflammation of the bronchial wall was first advanced by Stokes and adopted by Wilson Fox among others. They pointed out that the bronchial wall, as the result of the inflammation, loses its elasticity, contractility, and ciliary movement; the bronchi consequently dilate, and so an accumulation of secretion occurs. Yet if bronchitis leads to bronchiectasis, why is the former so common and the latter so rare? McPhedran[23] answers this by saying that "inflammation of the bronchi to be effective in causing dilatation must be destructive; it must destroy the structure which gives resisting power to the bronchial wall, namely, muscular tissue, elastic tissue, and cartilage." Another objection, however, is that bronchiectasis may develop without preëxisting bronchitis; and lastly, the walls of the dilatation are not infrequently found atrophied and without signs of inflammation.

5. Nervous theory: Lebert thought the loss of power of the bronchial walls was dependent rather more upon nervous influences than upon inflammation. Stewart and Gibson regard this theory as purely hypothetical and gratuitous, and point out that in analogous processes as aneurysm, varicose veins, and staphyloma posticum there is no reason to look for nervous causes but rather local nutritional changes.

[23] Osler's System of Medicine, Oxford, 1908, iii, 681.

6. Primary atrophy of the bronchial wall: This explanation of the origin of bronchiectasis was first advanced by Grainger Stewart in 1867, founded upon a series of pathological and clinical observations. In Stewart's opinion it offered a satisfactory explanation of the most important and commonest groups of cases which he terms primary, while he fully admits the existence of other secondary varieties. "The process then is to be regarded as analogous to the direct atrophic form of emphysema and not improbably to result from a constitutional possibly an hereditary effect."[24] In primary bronchiectasis the essential element is an atrophy of the bronchial walls; the cause for such atrophy is not yet understood, but it is probably connected with constitutional peculiarities. The walls of the bronchi being so thinned and weakened, yield to the ordinary air pressure, or it may be that deep and sudden inspiration or violent muscular exercise or the sudden expiratory efforts made while the glottis is closed in the act of coughing aid in the process of dilatation. The existence of dilatation favors the accumulation of mucus, and this in turn to inflammation and formation of villous processes, increased connective tissue, irritation of the cartilages, and to consolidation of the surrounding lung and pleuritic adhesions.

The secondary bronchiectasis may occur in the course of various morbid conditions of the surrounding lung tissue or be due to mechanical obstruction to the free passage of air in inspiration and expiration. The explanations of the pathogenesis of bronchiectasis advanced by most writers apply to these secondary cases: "How much influence to assign to each of these causes in any given case is difficult to determine."

7. Ewart's explanation: William Ewart[25] has pointed out that the common feature of all cases of bronchiectasis is faulty distribution of space between the air tubes and pulmonary tissue. Any excessive stress ultimately finds out the least resistant tissue, which is most often the pulmonary, and therefore becomes emphysematous; if, however, the bronchi are previously diseased they may suffer. In disease, therefore, other mechanical factors arise, namely: (1) Within the bronchi an accumulation of mucus and an antecedent or resulting degeneration of the bronchial wall; (2) changes induced in the lung tissue may bring about a faulty allotment in space, namely, (*a*) emphysema, much of which is effect, not cause; (*b*) collapse, which when occurring unevenly at one side of a bronchial tube may act as one of the agents of dilatation: (*c*) increase in the subpleural, perilobular, and interlobular stroma.

"As to the general mechanism of the dilatation we must again look for some elementary factor common to all varieties, and this we find in obstruction in the broadest sense of the word." Owing to the alternating direction of air currents an obstruction may lead

[24] Stewart and Gibson, loc. cit.

[25] Loc. cit.

to dilatation either on its proximal or on its distal side. The dilating force is usually not as in other tubes, as the alimentary tract, due to the pressure of an internal accumulation, but has its seat on the distal side of the dilatation; it is an aspirating not a forcing pressure. "The inspiratory traction made by the chest wall if it should fail to expand an obstructed lobule, might be transmitted to the delicate air tube adjoining the latter and might dilate it. Owing to the solidarity existing between all parts of the lung, this encroachment of bronchial space into the vacated pulmonary space may occur at a distance from the original collapse." The progressive increase in the dilatation may be brought about according to either the inspiratory or the expiratory hypothesis. In the former, according to Laennec, an abnormal inspiratory effort preceding cough throws a damaging stress upon the weakened parietes of the bronchial tube. The expiratory hypothesis has been advanced for bronchiectasis as for emphysema. In expiration with the glottis closed the pressure may rise to 80 mm. of mercury and in severe coughing to 110 mm. or more, while in quiet expiration it does not exceed 2 or 3 mm. During inspiration the air is sucked through the stenosis but in expiration the expelling force is often insufficient, for the expelling force in this case is represented only by the elasticity of the tissue lying beyond the constriction. If a mass of mucus is present it may act like a valve, so that air can get in much more easily than it can get out. Stagnation of the air results, the pressure becomes very high and remains so continuously. This is greatly assisted by attacks of coughing. Yet if we accept this we must answer the question why it is that bronchiectasis and emphysema are not universal inasmuch as we are daily subjecting our bronchial tree to an intense muscular strain with closed glottis. Evidently this immunity is dependent upon a perfect distribution of pressure in the healthy lung. Cough may be powerless to dislodge the secretion and yet propel it far enough to cut off the dilated alveolus from the main bronchus. The result of a recurring valvular obstruction of this kind would be not only continued fulness of the dilatation while the surrounding tissues are being relieved of much of their air, but a maintenance within it of the highest air pressure at the time when the air pressure in its vicinity is at its minimum. Hoping to obtain some light on this theory, I turned to the studies of Tendeloo on *Emphysema*.[25] In this I was disappointed, as there was nothing in these technical papers on the dynamics and statics of emphysema that I could find in any way applicable to the mechanism of bronchiectasis.

Ewart shows how cough, bronchial catarrh, interstitial pneumonia, pleuropneumonic fibrosis, and stenosis may each and all

[25] Studien über die Ursachen der Lungenkrankheiten, 1902 (Wiesbaden, Bergmann); ibid., Ergeb. d. inner. med. u. Kinderheilk, 1910, vi, 1.

bring about an abnormal distribution of air space between the tubes and pulmonary tissue. It must be confessed that after due consideration of the various theories advanced it would seem that Ewart's hypothesis is the broadest and the most logical.

CONCLUSIONS. 1. Bronchiectasis is a not infrequent clinical condition, and is too often mistaken for pulmonary tuberculosis.

2. The possibility of a foreign body or syphilitic stenosis must always be excluded as etiological factors.

3. Skiagrams are helpful in the case of a foreign body, but bronchoscopy should be carried out to exclude a foreign body and to treat a possible stenosis of a bronchus.

4. The etiology is manifold, but the inflammatory causes are the most common.

5. Of the various theories that advanced by William Ewart is the most rational and scientific. It considers a faulty distribution of air space as a predisposing factor common to all cases. The general mechanism of dilatation is found in obstruction in the broadest sense of the word.

SPONTANEOUS RUPTURE OF THE SPLEEN IN TYPHOID FEVER, WITH REPORT OF A CASE CURED BY OPERATION (SPLENECTOMY).

BY LEWIS A. CONNER, M.D.,

PROFESSOR OF MEDICINE IN THE CORNELL UNIVERSITY MEDICAL COLLEGE,

AND

WILLIAM A. DOWNES, M.D.,

ASSISTANT PROFESSOR OF CLINICAL SURGERY IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK CITY.

THE spontaneous rupture of the spleen in the course of typhoid fever is sufficiently rare to warrant the report of a case, more especially as in this instance it was possible to make the diagnosis and, by prompt operation, to save the life of the patient. Only 12 other cases are recorded in the literature. In 9 of these the condition was discovered at autopsy. In the 3 remaining cases it was found in the course of operation done for supposed intestinal perforation. None of these cases recovered.

A physician, aged thirty-six years, was admitted to the New York Hospital on February 20, 1913, with the diagnosis of probable typhoid fever. Up to the onset of his symptoms, seven days before, he had never been seriously ill in his life. He had never had malarial fever nor any other disease likely to lead to enlargement of the spleen. At the onset the symptoms were those of a catarrhal cold,

sore throat, and slight cough. With these were increasing fever, headache, general body pains, malaise, weakness, and troublesome nausea.

Physical Examination. Muscular, well-nourished body. High color and flushed face. Moist, slightly coated tongue. Throat somewhat congested. Chest well-developed. Lungs show everywhere normal resonance. Good vesicular, respiratory murmur. No adventitious sounds, except an occasional sonorous rhonchus. Heart normal in size and position. Apex-beat felt in fifth space, 8 cm. to left of the midsternal line. Sounds clear and normal in character. Action regular and strong. Pulse large, full, and slightly rapid. Palpable arteries normal. Abdomen full and soft. No rose spots. Liver dulness extends in mamillary line from the sixth rib to the free border. Liver edge not felt. Both kidneys indistinctly felt; not tender. Area of splenic dulness is considerably increased and extends from the eighth to the eleventh rib and anteriorly 3 cm. beyond the costal margin. The edge of the spleen is distinctly felt, even with quiet respiration. On deep inspiration it extends fully 4 cm. below the costal margin. It is unusually broad; its edge is blunt and rounded and its consistence noticeably firm and tense. Palpation of the spleen causes distinct tenderness. The extremities are normal. There is no enlargement of the superficial lymph nodes. On admission temperature was 100.4°; respirations, 22; pulse, 88.

February 21. The patient passed a restless night, with much headache and general discomfort, and these symptoms continued throughout most of the day. At 7.15 P.M. he complained of a sudden, sharp, stabbing pain in the left hypochondrium. This was soon followed by severe aching pain in the left shoulder, which radiated somewhat down the left arm. Soon after the onset of the pain he vomited a small quantity of clear fluid and broke into a profuse perspiration. The pain was so severe as to require an injection of morphine. The respirations were rapid and shallow; there was marked tenderness to pressure just below the costal margin, where the spleen could be distinctly felt, and slight rigidity of the upper part of the left rectus muscle. At times the pain was felt somewhat in the right hypochondrium.

February 22. The severe pain in the left side and left shoulder continued throughout the night, in spite of a second injection of morphine. When seen in the morning the patient looked much more seriously ill. His eyes were sunken, his features drawn and anxious, his respirations shallow and hurried. There was still distinct tenderness in the left hypochondrium and slight muscular rigidity, so that the spleen could not be felt distinctly. The area of splenic dulness, however, seemed larger than on admission. Elsewhere the abdomen was soft and showed no tenderness on palpation. At the base of the left chest posteriorly the respiratory

murmur was feeble, and a distinct friction sound could be heard both on inspiration and expiration. The spontaneous pain had lessened, but was aggravated by the slight dry cough that was present. The ache in the left shoulder and left supraclavicular fossa persisted.

February 23. The patient passed a restless, uncomfortable night, complaining chiefly of headache and nausea. At times he was slightly delirious. During the day his general condition and appearance improved much, and he was able to take and retain a fair amount of liquid food. The bowels were moved satisfactorily by an enema. The pain in the left side had ceased to be troublesome, but there was still slight tenderness in the left upper quadrant. The physical signs in the chest were unchanged, and it was still impossible to determine the nature of the violent attack he had had two days before. The occurrence of a pulmonary infarct was suspected, but neither the symptoms nor the physical signs were sufficiently characteristic to justify that diagnosis. The extremities showed no indications of thrombophlebitis.

February 24. The patient's general condition had still further improved and he passed a comfortable day and night and seemed to be settling down to a fairly normal typhoid course. Although the Widal test was still negative, blood cultures taken on February 21 showed a Gram-negative bacillus which resembled the Bacillus typhosus, and which two days later was identified positively as such.

On the morning of February 25 the patient awoke refreshed after a comfortable night. At 8.30 A.M., however, he had an attack of coughing and immediately afterward complained of the same severe pain in the left hypochondrium and left shoulder. This pain continued throughout the morning, and was accompanied by profuse sweating and by the same startling change in appearance and general condition. When seen by one of us (Conner) about 11.30 A.M., he had, in even more marked degree, the sunken eyes, the pinched features, and anxious look that had characterized his first attack. His pulse was rapid, small, and soft; his respirations also were rapid, the skin was covered with cold sweat, and he complained of weakness and nausea. It was evident that something serious had happened, and that his condition was growing progressively and rapidly worse. Examination of the chest showed no change from that of the preceding days. Aside from some diminution of the respiratory murmur at the left base posteriorly and a few rales the pulmonary signs were normal. There was dulness on percussion over the greater part of the left side of the abdomen and in the left flank, and some rigidity and tenderness in the left upper quadrant. The rest of the abdomen was soft and while having a somewhat boggy feel, was not tender. The liver dulness was normal. Drs. William A. Downes and S. W.

Lambert were called in consultation, and it was agreed by all of us that the symptoms indicated a rupture of the spleen. This diagnosis was arrived at by considering the location of the pain, tenderness, and muscular rigidity; by the absence of signs pointing toward other likely complications, such as intestinal perforation and pulmonary infarction, and by the fact that the spleen had been recognized as being unusually large and tense for the early days of typhoid fever. With the hope of obtaining some confirmation of severe hemorrhage a blood examination was made about three and a half hours after the onset of the pain, and when the symptoms pointed strongly to an alarming loss of blood. The examination gave the following results: Red cells, 5,280,000; hemoglobin (Sahli), 85 per cent.; leukocytes, 35,000.

In spite of these apparently inconsistent blood-findings an immediate exploratory operation was decided upon, and at 1.45 P.M. (five and a quarter hours after the onset of the symptoms) the patient was taken to the operating room. The temperature, which at 8 A.M. had been 102.8°, was 100°, respirations 32, pulse 118. Dr. Downes, under local anesthesia, opened the abdomen by a vertical incision through the middle of the left rectus muscle. Upon opening the peritoneum the abdomen was seen to contain a large amount of blood. The patient was therefore given nitrous oxide gas and ether (by Dr. Thomas L. Bennett) and the incision was rapidly enlarged to an extent of eight inches. A tremendous quantity of fresh and clotted blood, estimated at from one and a half to two quarts, escaped from the abdomen. The left hand was passed immediately to the pedicle of the spleen which was grasped between the index and middle fingers, and the spleen delivered through the wound with the right hand. At this point the pedicle was caught with a long, straight, rubber-covered clamp placed close to the spleen. The vessels were then ligated, about two inches proximal to the clamp, with No. 2 chromicized catgut. The larger blood-clots were rapidly removed; one old and laminated clot, fully an inch thick, conforming to the size and shape of the phrenic surface of the spleen, was found high up under the diaphragm. The abdomen was closed by layer sutures without drainage. Time of operation, twenty minutes.

When the hand was first passed behind the spleen, lying in its bed, a rent in the capsule, fully three inches in length, was encountered, running along the posterior border, and during the manipulation this rent was so enlarged by the time the organ was brought out of the wound that the capsule had been stripped from almost half its surface.

In spite of his critical condition on the operating table, which required an intravenous infusion of salt solution, the patient improved steadily during the succeeding twelve hours. His loss of fluid was replaced by saline solution given by hypodermoclysis

and by the Murphy "drip." At 10 P.M. the hemoglobin percentage had fallen to 62 and his leukocytes numbered 68,000. On the following morning (February 26) the pulse had fallen to below 100 and his general condition was satisfactory. At 2 P.M. an examination of the blood gave the following results: Red cells, 2,810,000; hemoglobin, 58 per cent.; leukocytes, 36,400.

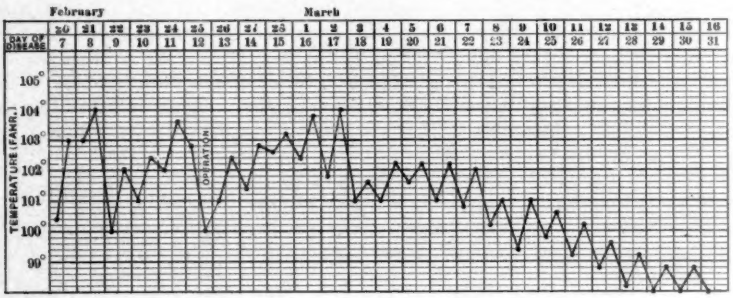


Chart of case of spontaneous rupture of the spleen in typhoid fever.

On March 2 the patient complained of some pain in the left shoulder. There was no cough or other symptoms, but examination of the left chest posteriorly revealed an area of dulness over the middle portion of the lower lobe and, corresponding to this, a small area over which bronchial breathing and bronchophony could be heard. At that time the extremities showed no signs of thrombophlebitis.

March 3. Widal test positive.

March 5. Slight tenderness on pressure over the lower part of the left calf. The median basilic vein of the right arm was thrombosed at a point distal to the place of the infusion puncture at the time of the operation, and showed as an indurated, tender cord 8 cm. long. The area of bronchial breathing in the left lower lobe had disappeared, but over the lower half of the lower lobe there was marked dulness, absence of breath sounds and fremitus, and distant nasal voice. There was slight cough and occasional pain in the left axilla, but no expectoration.

During the next few days the tenderness in the left calf became more pronounced and more extensive, and a similar area of tenderness appeared in the right calf, together with an indistinct elongated area of induration. These indications of thrombophlebitis gradually subsided, as did also the signs of pulmonary infarction.

By March 15 the temperature had reached normal and the patient was convalescent.

On March 31 he was able to leave the hospital, and one month later had regained his lost weight and seemed in almost his usual health.

TABLE OF BLOOD EXAMINATIONS.

Date.	Red cells.	Hemoglobin, per cent.	Leukocytes.	Polymorphonuclears.	Lymphocytes and large mononuclears.	
Feb. 20, 1913	.....	.....	8,800	71	17	11
Feb. 22,	.....	.....	13,400	60	30	10
Feb. 25, 12 M.	5,280,000	85	35,000	87	13	
Feb. 25, 10 P.M.	.....	62	68,000	91	9	
Feb. 26, 2 P.M.	2,800,000	58	36,400	86	14	Normoblasts.
Feb. 28	.....	.....	24,800	67	22	10 Myelocytes and normoblasts
Mar. 1	.....	58	30,000	83	17	Normoblasts.
Mar. 12	.....	62	15,800	82	17	
Mar. 23	.....	71				

Pathological Report (Dr. Tytler). The spleen is of about normal shape, swollen, and firm, and measures 14 cm. in length by 11 cm. maximum width by 7 cm. maximum thickness. Weight, 375 grams. The anterior border shows one shallow notch near the anterior extremity. The capsule shows an extensive tear starting about the middle of the anterior border, following that border to the posterior extremity, thence obliquely across the renal surface to the middle of the posterior border, and thence along that border almost to the anterior extremity. The flap formed by this tear is loose and completely separated from the diaphragmatic surface. The capsule itself is thin, smooth, and transparent everywhere.

The separate mass of blood-clot received was removed from the diaphragmatic surface. It is disk-shaped and measures about 12 cm. in greatest diameter by 2 to 3 cm. in thickness. It is firm, dark reddish brown, and on section shows a definite laminated structure.

The surface of the spleen over the area from which the capsule was separated is smooth, dark red in color, and shows no laceration or rupture. On section the spleen cuts readily, leaving a swollen, congested, slightly indurated cut surface in which the lymph follicles and trabeculæ can just be distinguished.

Microscopic sections show the spleen pulp much congested and packed with large phagocytic endothelial cells both in and between the sinuses. The endothelial lining of the sinuses is swollen and shows some proliferation. Small leukocytes are seen in the sinuses and between them. The pulp cords are compressed and the lymphocytes relatively fewer than natural. The lymph follicles are of about natural size and show no significant lesions. The whole picture corresponds to the usual findings in the spleen of typhoid fever.

The capsule in the section examined (from the hepatic surface) shows no abnormalities. It is of natural thickness, and consists of mature fibrous tissue, with no cellular infiltration.

DISCUSSION. The reasons for the diagnosis of rupture of the spleen have been given. The condition probably would not have been recognized had it not been for the fact that attention had been directed to the spleen by reason of its unusually large size and firm consistence. When once the possibility of its rupture had been thought of the symptoms seemed to correspond so perfectly with what might be expected under such circumstances that the diagnosis could be made without much hesitation.

Two further points of interest deserve mention. The discovery at operation of a layer of old, laminated clot lying directly over the dorsum of the spleen made it certain that the acute symptoms which appeared three days before the day of operation indicated the time of the first rupture of the splenic capsule. These symptoms had entirely subsided before the second attack of pain, which followed immediately upon an attack of coughing. At this time evidently there was either an increase in the rupture of the capsule or a displacement of the old clot and subsequent uncontrollable bleeding from the site of the old tear. The subsidence of the symptoms after the first attack of pain suggests the possibility that, rarely, a rupture of the capsule of the spleen may be followed by spontaneous cessation of the bleeding and recovery.

The second point of interest relates to the character of the blood, as shown by examination, at a time when all the symptoms indicated an alarming internal hemorrhage. At that time the red cells numbered over 5,000,000 to the centimeter and the hemoglobin percentage was 85. This apparent inconsistency was interpreted as meaning that the hemorrhage had occurred so rapidly that there had not been time for the circulating blood to take up any appreciable amount of fluid from the tissues, and that the blood in circulation, while greatly reduced in volume, was as yet unchanged in consistence. On the day after the operation the red-cell count was 2,800,000 and the hemoglobin was 58 per cent. It is interesting to note that although before the operation the red cells showed no material change in concentration, the circulating leukocytes had already increased to 35,000. That rapid, severe hemorrhage is followed by a rise in the number of leukocytes and in the percentage of polymorphonuclear cells is well recognized; but we have been able to find no mention of the fact, illustrated in the present case, that this increase in the leukocytes occurs much earlier than do the other characteristic blood changes—namely, the fall in the number of red cells and in the percentage of hemoglobin.

Spontaneous rupture of the acutely swollen spleen is a rare occurrence, but has been encountered in the course of various fevers. In tropical malarial fever it has been seen in a considerable number of cases. More rarely it has been observed in typhus, relapsing,

and typhoid fever. In the case of the last-named disease, Melchior[1] has been able recently to collect but twelve authentic instances of such spontaneous rupture.[2] Since his careful review of the subject no further cases have appeared in the literature. The rarity of this complication in typhoid fever may be further shown by the following statistics: Curschmann[3] found two instances of it among 577 autopsies in cases of typhoid. Among 2000 typhoid autopsies in the Munich Pathological Institute it was observed 5 times (one of these was in a case of abscess of the spleen[4]). Among 474 fatal cases of typhoid observed in St. Jacob's Hospital, in Leipzig, between the years 1880 and 1907, no instance of rupture of the spleen was seen.[5]

Bryan,[6] of Richmond, Va., has reported an interesting case of spontaneous rupture of the spleen in the course of typhoid fever, and has attempted to assemble all the reported cases; but in his collection of 28 cases he has included indiscriminately cases of ruptured spleen in typhus, relapsing, and malarial fever as well as in typhoid fever.

All of the 12 cases of spontaneous rupture in typhoid collected by Melchior occurred in males. Ten of those were adults, and 2 were boys, aged respectively eight and ten years.

As regards the time of the disease at which the rupture occurred, in 5 of the 13 cases (including our own) the signs of rupture appeared during or at the end of the second week; in 2 cases during the third week; in 1 at the end of the fifth week; in 1 during convalescence, and in 1 during an apparent relapse. In 3 cases there was no information upon this point.

The site of the rupture is mentioned in 7 of the 13 cases. In 3 instances this was in the region of the hilum; in 2 cases, near the lower pole; in 1 on the diaphragmatic surface, and in 1 (our own) along the posterior border. Usually the tear has been linear. In 1 case it was stellate; in 1 angular; in 1 it extended almost around the spleen near its middle. In most of the cases the tear has involved not only the capsule but the parenchyma as well. In our own case, however, and in that of Kammerer's, the tear was confined to the capsule; but in spite of this fact the hemorrhage in both cases was enormous.

[1] Die Spontanrupturen der Milz in Verlauf und Gelfoge des Typhus, abdominalis, Centralbl f. d. Grenzgeb. d. Med. u. Chir., 1911, xiv, 810 and 897.

[2] Melchoir's collection includes thirteen cases, but one of these (Case 9) obviously cannot be regarded as an instance of spontaneous rupture.

[3] Der Unterleibstyphus, Wien, 1893.

[4] Holscher, Ueber die Komplicationen bei 200 Fällen von letalem Abdominaltyphus, Münch. med. Woch., 1891, p. 43.

[5] Berg, Statistik der im Krankenhause St. Jakob in Leipzig in den Jahren. 1884–1893, behandelten Fälle von Typhus abdominalis, Inaug. Diss., Leipsig, 1893. Piokowsky, Statitik der in Krankenhause St. Jakob in Leipzig während der Jahre 1893–1907, behandelte Fälle von Typhus abdominalis, Inaug. Diss., Leipsig, 1907.

[6] Spontaneous Rupture of the Spleen in the Course of Typhoid Fever, Ann. Surg., 1909, l. 857.

The duration of the symptoms in the cases of rupture of the spleen has varied from a few hours to two or three days. In Erichsen's case death is said to have occurred "in a few minutes." In 9 of the 12 cases collected by Melchior the condition was recognized only at autopsy. In the 3 remaining cases (Kammerer, West and Dudding, Bryan) the rupture of the spleen was discovered in the course of an operation done for supposed intestinal perforation. None of these cases recovered.

The *symptoms* of rupture of the spleen fall into two quite distinct groups: (1) the local symptoms of the rupture and of irritation of the neighboring peritoneum by the extravasated blood, and (2) the general symptoms of severe internal hemorrhage. In most of the cases described pain seems to have been the first symptom, although the location and character of the pain have usually not been given in much detail. In our own case there was severe pain referred to the splenic region, and also very severe pain in the left shoulder and in the left supraclavicular fossa. In West and Dudding's case the pain is said to have been referred to the central part of the abdomen. In addition to the pain there had usually been some tenderness and muscular rigidity in the left upper quadrant of the abdomen. In one of Chrostowski's cases the tenderness was extreme. The general symptoms, due to the progressive loss of blood, have been increasing collapse, pallor, rapid pulse, with falling temperature, restlessness, thirst, etc. In one case (Bryan) instead of a fall in temperature there was a rise to 106°.

The *diagnosis* of rupture of the spleen in the course of typhoid fever rests upon the association of the signs of local trouble in the left upper quadrant of the abdomen (pain, tenderness, muscular rigidity), with the evidences of progressive internal hemorrhage. In most cases the diagnosis ought not to be difficult if only the possibility of the occurrence of such a rupture is borne in mind. In our own case this possibility was suggested by the fact that the spleen had been recognized as being unusually large for the early days of typhoid fever. The difficulties of diagnosis will naturally be greatly increased in cases which are already gravely ill or in which delirium or great apathy mask the local symptoms. In the three earlier cases operated upon the condition suspected was that of intestinal perforation or perforation and hemorrhage.

Prognosis. Although all of the twelve previously reported cases have died, the evidence in our case that the first rupture occurred three days before the appearance of the symptoms which led to the operation, suggests the possibility that such a rupture may in rare instances be followed by spontaneous recovery. In general, it may be said, however, that the only chance of recovery lies in the prompt recognition of the condition and in immediate operation. In most instances the loss of blood has been so rapid and severe

that the delay of even a few hours would greatly imperil the chance of recovery, so that in any case in which there is a reasonable probability that the condition is one of rupture of the spleen the safest procedure would seem to be the making of a small exploratory incision under local anesthesia, as was done in the present case. If a rupture is found there seems to be no question that the prompt removal of the organ is greatly to be preferred to any attempt to check the bleeding by merely packing the wound in the spleen.

A summary of the twelve cases already reported is as follows:

CASE I.—Nückel,[7] 1839. A robust man, aged twenty-five years, was seized with diarrhea fourteen days before death. Two days before death he took to his bed with abdominal pain. Then followed collapse, pallor, sweating, cold extremities, and death.

Autopsy. Large, soft spleen, in the lower part of the outer surface of which was an angular tear three to four lines wide. Left hypochondrium filled with blood which extended throughout the left side of the abdomen as far as the true pelvis. There were numerous ulcers in the ileum.

CASE II.—Heimann,[8] 1843. In an account of a typhoid epidemic in Moscow is a brief reference to a case in which the enlargement and softening of the spleen was so great that the capsule, stretched to its utmost, finally burst and the softened material almost filled the left side of the abdominal cavity.

CASE III.—Erichsen,[9] 1861. A vigorous man, who had passed through typhoid fever and was almost ready to be discharged, suddenly collapsed and died "in a few minutes." The autopsy showed the abdomen to be filled with an enormous quantity of liquid and clotted blood. The pancreas was surrounded by a mass of clot as large as a child's head, which extended to the hilum of the spleen. The spleen formed a flaccid sac, seven inches in diameter, composed of grumous, confluent, livid-red parenchyma, in which no trace of normal splenic structure could be seen. In the region of the hilum were three or four tears about one inch in length. Liver was cirrhotic, enlarged, and anemic.

CASE IV.—Delafield,[10] 1875. Boy aged eighteen years, two weeks before had caught cold; was seized with cough, fever, coffee-ground sputa; had a little pain in the right side of the chest. Was worse every afternoon. No diarrhea, headache, or epistaxis. October 27: Tongue clean; pulse, 100; temperature, 99¾°; bowels regular; urine 1010, no albumin. Coarse rales over both lungs. October 29: Pulse, 100 to 112; temperature, 99¾° to 102¼°. October 30: Pulse 114 to 122; temperature, 100° to 103½°. October 31:

[7] Ruptur der vergrösserten und erweicherten Mils, Med. Zeit. des Vereins f. Heilkunde in Pr., 1839, No. 19; Ref. Schmidt's Jahrb., 1840, xxviii, 49.

[8] Der Typhus in Mosjauer Militärspital während der Herbst und Wintermonate des Jahres, 1840–1841, Hufeland's Jour. der prakt. Heilkunde, 1843, xcvi, 93.

[9] Zwei Fälle von innerer Blutung, St. Petersburger med. Zeitsch., 1861, i, 71.

[10] Through the courtesy of Dr. Delafield, these notes were copied from his case-book.

Pulse, 104; temperature, 100¼°. November 1: Pulse, 96 to 120; temperature, 99° to 98½°. November 2: Pulse 98 to 120, temperature 99 to 98½°. November 3: Improving today, sat up. November 7: Complained of weakness; stayed in bed. November 10: Suddenly grew much worse. At 2 P.M., pulse, 145; temperature, 104¼°. At 8 P.M., Pulse, 144; temperature, 105½°. November 11, at 2.30 A.M. patient was found in the hall dying. Died at 3 A.M. *Autopsy:* Brain had a slight increase of serum beneath; heart normal; lungs, moderate bronchitis; liver normal. Spleen weighed fourteen ounces with a large rupture extending all around it at about its middle. In the peritoneal cavity there was a large amount of blood. Large intestine normal. Along the entire length of the ileum solitary and aguinated glands very much swollen and a few of them ulcerated. Small nodules in mucous membrane. Mesenteric glands very much swollen.

CASE V.—Wittmann,[11] 1876. Boy aged ten years. Admitted to the hospital on sixth day of illness. Persistent high fever, delirium, and bleeding from mouth and bowels. Tenderness over the cecum and spleen. Splenic dulness much increased. From the eighth day of illness on there was increasing tenderness of abdomen, especially in the region of the spleen. On the thirteenth day there was a rapid fall of the persistently high temperature to subnormal, symptoms of acute collapse, and death. *Autopsy:* The abdominal cavity contained one and one-half pounds of liquid and clotted blood. Spleen enlarged fourfold, soft and pale. On the outer border there was a tear one inch deep and two and one-half inches long, beginning near the hilum, running to the outer border, and ending on the upper surface. A second shallower and shorter tear began at the hilum, where it was joined with the first tear and extended down toward the tip of the spleen. Peyer's patches were swollen and in part ulcerated. The mesenteric glands much enlarged.

CASE VI.—Chrostowski,[12] 1885. Blacksmith, aged twenty-seven years. Had been ill several days when first seen. Temperature, 40.3° C.; pulse, 100; respirations, 24. Two days later became delirious; desperately attempting to get out of bed. Great tenderness in the region of the spleen. High temperature and rapid pulse and respirations. Abdomen enormously enlarged. Became unconscious during the night and died the next morning. *Autopsy:* The spleen was six times its usual size; the outside was covered with thick, dark blood. The vertical rupture of the spleen was 8 to 10 cm. long.

CASE VII.—Chrostowski,[13] 1885. Male, aged eighteen years. Ill in bed six days before admission to the hospital. On twenty-

[11] Abdominaltyphus mit Milsruptur, Jahrb. f. Kinderheilk., 1876, ix. 329.

[12] Ruptures of the Spleen in General, and Two such Cases Occurring in Typhoid Fever, Hoyersche Denkschrift, Warschau, 1885 (Polish); Ref. Virchow-Hirsch, 1885, ii. 30.

[13] Loc. cit.

second day the temperature still was high; patient was delirious. The next day the temperature fell to normal and the patient seemed better, but on the following day he died. *Autopsy* showed the spleen considerably enlarged and surrounded by thick, coagulated blood. The spleen showed a rupture of the capsule 3 cm. long, which extended into the splenic pulp.

CASE VIII.—Aaser,[14] 1898. Man, aged twenty years. Patient had typhoid fever of fourteen days' duration, and died a half-hour after admission to the hospital. *Autopsy* showed a rupture of the spleen so extensive that a portion of the organ was almost completely severed from the rest.

CASE IX.—Kammerer,[15] 1902. The patient was in the third week of typhoid fever. No trauma. Sudden restlessness and signs of internal hemorrhage. Diagnosis of intestinal perforation. *Operation:* Large amount of blood in belly. Intestine intact. Greatly enlarged spleen surrounded by clot. Capsule showed a tear four inches long, through which the splenic tissue protruded. Extirpation of spleen. Death after twelve hours. The rupture involved the capsule only.

CASE X.—Craig,[16] 1904. Soldier, aged twenty-three years. Illness of eight days before admission to the hospital on September 12. Temperature reached normal before October 3. On that day the patient felt cold and sleepy. Temperature subnormal. Slight delirium. Next day had severe pain which was referred to the left hypochondrium. This pain increased on the following day. Gradual collapse and death on October 7. *Autopsy:* Typhoid ulcers in the ileum. Coils of small intestine were adherent and covered with purulent exudate. Appendix was inflamed. Spleen was greatly enlarged (20 by 11 cm.), and surrounded by a great mass of blood. Tear in the spleen was 3 cm. long and 1 cm. deep, from which the splenic tissue protruded.

CASE XI.—West and Dudding,[17] 1906. Soldier, aged twenty-five years. Was admitted to the hospital on the third day of his illness. Fever ran a mild course, with few symptoms, until the ninth day (March 3), when at 8.45 A.M. he complained of severe pain in the middle of the abdomen. When seen fifteen minutes later he was in a collapsed condition, somewhat restless, with a rapid, weak pulse, and with the abdomen tender, distended, and tympanitic. Perforation was suspected. *Operation:* Abdomen was filled with blood. No perforation discovered. Spleen suspected as being the source of the bleeding, but because of the bad condition of the patient the abdomen was closed. Death occurred ten

[14] Milzruptur ved tyfoidfeber, Tidskr. f. d. norske Laegefor, Christiania, 1898, xviii, 565.
[15] Hemorrhage from the Spleen in Typhoid Fever, Ann. Surg., 1903, i, 288.
[16] Rupture of the Spleen: Report of Two Cases, Med. News, 1904, lxxxiv, 780.
[17] A Case of Enteric Fever with Spontaneous Rupture of the Spleen. Jour. Royal Army Med. Corps, London, 1906, vii, 183; Ref. Lancet, 1906, ii, 1230.

minutes later. *Autopsy:* Spleen was greatly enlarged, weighing two pounds two and one-half ounces. Capsule showed a tear three inches long on the diaphragmatic surface, and was extensively separated by a clot. Typhoid ulcers in the ileum and colon.

CASE XII.—Bryan,[18] 1909. Man, aged thirty-one years. Was admitted to the hospital November 2 having been ill for one week with fever and headache. Complained of some pain on the left side under the ribs. Ran a persistently high fever for the next twelve days. No trauma. On the evening of November 14 the temperature became higher than usual (106°), and the pulse rapid and weak. The face was pinched; nose and extremities were cold, there was moderate dyspnea. The belly was hard, resistant, and tympanitic, but not distended. *Diagnosis:* Perforation and hemorrhage. *Operation:* The abdomen was opened along the outer border of the right rectus muscle. No perforation was found, although thickened Peyer's patches were evident. Blood in large quantities was found in the pelvis and in the region of the spleen. Spleen was removed. In spite of saline infusion and other measures to combat the shock and loss of blood, death followed one hour later. The spleen measured 18 by 9 cm., and weighed fourteen and two-third ounces. The rupture, situated at the lower pole, was stellate, everted, and crater-like. It covered an area 2.2 by 3.8 cm., and extended into the tissue of the organ.

A STUDY OF THE PATHOLOGY OF THE THYROIDS FROM CASES OF TOXIC NON-EXOPHTHALMIC GOITER.

BY LOUIS B. WILSON, M.D.,

DIRECTOR OF LABORATORIES, MAYO CLINIC, ROCHESTER, MINNESOTA.

(Presented before the State Medical Society, Minnesota, October 2, 1913).

INRODUCTION. That a secretion from the thyroid gland is the cause of the toxic symptoms in goiter has not yet been positively proved. Indeed, the proof is still somewhat incomplete that any secretion from the thyroid may be found in the circulating blood. However, evidence is slowly accumulating which it seems likely will ultimately prove both these propositions beyond peradventure.

Five years ago[1] I gave a detailed analysis of the pathology of 259 thyroids removed from patients listed clinicaly as "exophthalmic goiter" from January 1, 1905, to May 10, 1908, and,

[18] Loc. cit.

[1] AMER. JOUR. MED. SCI., December, 1908, pp. 851–61.

in addition, a review of the pathologic reports of 35 cases similarly listed in the Mayo Clinic prior to January 1, 1908. I pointed out that above 76 per cent. of these glands showed primary parenchymatous hypertrophy and hyperplasia, and that in general, the length and severity of the case history could be predicated from a knowledge of the pathologic findings. The margin of above 20 per cent. of the cases on the "exophthalmic goiter" list whose thyroids did not show primary hypertrophy and hyperplasia of the parenchyma were explained at the time by the supposition that they were either "patients who have recovered from their toxic symptoms and are now suffering principally from long, previously acquired heart or nerve lesions," or that they were "recently developed, very mild, or moderately mild cases of long standing." The fairly accurate estimates of the clinical condition from the pathologic data were made on the hypothesis "that the symptoms of Graves' disease are associated with increased absorption of an increased secretion of the thyroid."

Since this report, it has become possible more intelligently to interpret the pathologic pictures because of the increasing clearness of our conception of the various clinical types of goiter. From an extensive and detailed study of all types of goiter, Plummer[2] has recently called attention to the fact that clinically there are two distinct groups of toxic goiters: (1) exophthalmic and the other (2) toxic non-exophthalmic. The former, I have demonstrated pathologically, all show primary hypertrophy and hyperplasia of the parenchyma as the dominant pathologic change in the thyroid. Allowing for a small margin of error on both the part of the pathologist and of the clinician, all cases of clinically exophthalmic goiter coming to operation in the Mayo Clinic during the years 1911 and 1912 showed primary hypertrophy and hyperplasia of the parenchyma of the thyroid and practically no cases of toxic non-exophthalmic or of non-toxic (*i. e.*, simple) goiter showed any such pathologic change.

Thus the evidence of the constant association of primary hypertrophy and hyperplasia of the thyroid with the symptoms of true exophthalmic goiter would seem to be fairly conclusive. Our previous communications have, however, touched but lightly on the pathology of the thyroid in cases of toxic non-exophthalmic goiter, and it is this phase of the subject to which I wish herein to call attention.

Plummer[2] has shown that about 23 per cent. of all goiters reported as non-hyperplastic are of the toxic non-exophthalmic type, while the remainder are atoxic (simple) goiters. He notes, further, that "Patients coming under observation with non-hyperplastic toxic goiter give a history of having first noticed the goiter at the average

[2] Jour. Am. Med. Assoc., August 39, 1913, pp. 650–51.

age of twenty-two years and the evidence of intoxication at the average age of 36.5 years. The corresponding ages for hyperplastic goiter are respectively 32 and 32.9 years. That non-hyperplastic goiter is noted ten years earlier in life than hyperplastic goiter, and that 14.5 years elapse between the appearance of non-hyperplastic goiter and the development of notably toxic symptoms, while the constitutional symptoms are noted but a few months later than the goiter in patients affected with hyperplastic goiter, is alone sufficient to show that we are dealing with at least two distinct pathologic and clinical groups. That one is not the sequence of the other is self-evident."

Plummer further divides the intoxications from non-hyperplastic goiter into two merging groups: "(1) A group in which the cardiac toxin predominates and in which the clinical picture closely resembles, and, in many instances, cannot be differentiated from, the cardiovascular complex resulting from alcoholic, luetic, septic, and other well-known toxins; (2) A group more closely presenting the picture of Graves' disease and including the cases that have been erroneously so diagnosed by the mass of the profession."

I wish to present in this paper the results of a somewhat intensive study of the thyroids from approximately equal numbers of cases taken consecutively in our series, the only selection being made consisting in the exclusion of cases of which full data were not at hand. This includes:

1. 431 thyroids removed from cases of true exophthalmic goiter during the years 1911 and 1912.

2. 373 thyroids removed from as many cases of non-toxic (*i. e.*, simple) goiter during the year 1912.

3. (*a*) 129 thyroids removed from toxic non-exophthalmic cases during the years 1910, 1911, and 1912, and clinically in Plummer's sub-group 2, *i. e.*, "cases with symptoms closely approaching the picture of Grave's disease," (*b*) 155 thyroids removed from toxic non-exophthalmic cases during 1911 and 1912, and clinically in Plummer's sub-group 1, *i. e.*, "cases in which the clinical picture closely resembles and, in many instances, cannot be differentiated from the cardiovascular complex resulting from alcoholic, luetic, septic and other well-known toxins", and (*c*) thyroids from 90 cases similar to the last but of more mild or doubtful toxicity. The non-exophthalmic cases of clinical group 2 were included on the "exophthalmic goiter" list for 1910, 1911, and 1912 because of their resemblance to true exophthalmic goiter, while the cases in clinical group 1 were included on the "simple goiter" list because, though toxic, they did not resemble symptomatically the cases of true exophthalmic goiter. The thyroids from these cases have all been carefully analyzed as to their gross and microscopic pathology. A summary of the more important analytic data is presented in the following table:

Comparison of Pathologic Grouping of Thyroids from Cases of Exophthalmic, Toxic Non-exophthalmic, and Atoxic (Simple) Goiter.

	Percentage distribution.					Average age at operation.					Average duration of goiter before operation.					Average weight of portion of gland removed.				
	Exoph. goiter. "Exoph. list," 1911–12. 431 cases	Toxic goiter clinic, Group 2. "Exoph. list," 1910–12. 129 cases	Toxic goiter clinic, Group 1. + "Simple list," 1911–12. 155 cases = 374 cases	Toxic goiter clinic, Group 1. † "Simple list," 1912. 90 cases	Atoxic (simple) goiters. "Simple list," 1912. 373 cases	Exoph. goiter. "Exoph. list," 1911–12. 431 cases	Toxic goiter clinic, Group 2. "Exoph. list," 1910–12 129 cases	Toxic goiter clinic, Group 1. + "Simple list," 1911–12. 155 cases = 374 cases	Toxic goiter clinic, Group 1. † "Simple list," 1912. 90 cases	Atoxic (simple) goiter. "Simple list," 1912. 373 cases	Exoph. goiter. "Exoph. list," 1911–12. 431 cases	Toxic goiter clinic, Group 2. "Exoph. list," 1910–12 129 cases	Toxic goiter clinic, Group 1. + "Simple list," 1911–12. 155 cases = 374 cases	Toxic goiter clinic, Group 1. † "Simple list," 1912. 90 cases	(Atoxic simple) goiters. "Simple list." 1912. 373 cases	Exoph. goiter. "Exoph. list," 1911–12. 431 cases	Toxic goiter clinic, Group 2. "Exoph. list," 1910–12. 129 cases	Toxic goiter clinic, Group 1. + "Simple list," 1911–12. 155 cases = 374 cases	Toxic goiter clinic, Group 1. † "Simple list," 1912. 90 cases	Atoxic (simple) goiter. "Simple list," 1912. 373 cases
	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Years.	Years.	Years.	Years.	Years.	Years.	Years.	Years.	Years.	Years.	Grams.	Grams.	Grams.	Grams.	Grams.
A Early primary parenchymatous hypertrophy and hyperplasia	4.0	..	..	..	..	25.0	..	..	..	..	0.3	..	..	..	..	38				
B Advanced primary parenchymatous hypertrophy and hyperplasia	43.0	..	..	..	..	31.7	..	..	..	..	0.9	..	..	..	..	61				
C Regressing primary parenchymatous hypertrophy and hyperplasia	52.5	..	..	..	..	40.7	..	..	..	..	3.5	..	..	..	..	51				
Average of total parenchymatous hypertrophy and hyperplasia	99.5	..	..	..	0.5	35.9	..	..	..	..	2.3	..	..	..	..	55				
D Secondary regeneration of atrophic parenchyma of "colloid" goiter	..	50	17	9	9.0	..	34.0	32.0	38.0	31.0	..	6.9	15.3	8.0	9.6	..	67.0	100	153	143.0
E Fetal adenomas	..	12	7	10	5.0	..	39.0	47.0	39.0	38.0	..	4.4	5.8	13.6	12.5	..	68.0	97	139	122.0
F Degenerating fetal adenomas	..	33	14	18	18.0	..	43.0	50.0	48.0	40.0	..	12.6	22.7	24.2	13.1	..	91.0	186	190	129.0
Average of total fetal adenomas	..	45	21	28	23.0	..	41.0	48.9	44.7	39.7	..	8.8	18.0	20.5	13.0	..	83.7	162	172	127.5
G Adult "colloid" adenomas	..	3	21	19	23.0	..	45.0	44.0	43.0	39.0	..	17.7	15.2	14.5	14.3	..	139.0	184	206	147.0
H Atrophic parenchyma, ("colloid") thyroids, "adenomatoses," etc.	..	2	41	44	44.0	..	52.0	46.0	41.0	37.0	..	12.0	20.2	16.5	14.5	..	140.0	196	188	164.0
Average of total colloid goiters, adult parenchyma	..	5	62	63	67.0	..	47.5	45.0	41.6	37.5	..	14.0	18.7	16.0	14.4	..	139.0	193	193	159.0

DISCUSSION OF DATA. *Percentage Distribution.* The distribution of the thyroids from each of the four clinical groups into the eight pathologic groups shows the following interesting points:

1. Practically all of the 433 cases of true exophthalmic goiter show some stage of primary hypertrophy and hyperplasia; of the thyroids; 4 per cent. are in an early stage, 43 per cent. in an advanced stage, and 52 per cent. in a regressing stage. As I have previously pointed out,[3] this regression may be due to (*a*) the self-destruction of the parenchyma of the gland through the over-functioning of hyperplastic tissue, or (*b*) the destruction of the parenchyma through surgical interference (*e. g.*, ligation of the thyroid arteries which had been performed in a large percentage of the cases in this series).

2. Fifty per cent. of the thyroids from the toxic non-exophthalmic cases of clinical group 2 (*i. e.*, those which resemble more or less the true exophthalmic goiter cases) showed marked evidences of regeneration of the parenchyma (group D). I have elsewhere noted that regeneration of previously atrophic parenchyma of the thyroid is often a marked process which can usually be differentiated from primary parenchymatous hypertrophy and hyperplasia by (*a*) the abundant presence of atrophic parenchyma within large acini, (*b*) the development of numerous new acini within one or more portions of the walls of the old large colloid-filled acini and which early fill with dense colloid, and (*c*) the development of multiple layers of relatively small parenchyma cells within the large colloid-filled acini, which are distinguished from primary parenchymatous hypertrophy and hyperplasia by the smaller size of the parenchyma cells and the absence of papillæ.

3. Seventeen per cent. of the thyroids from the positively toxic cases in clinical group 1 (*i. e.*, those in which the clinical picture appears to be the result of a cardiac toxin) are of the regenerative (D) type. Though this percentage is but one-third that of the preceding group, it is still nearly twice that shown by the thyroids of doubtful toxicity and by the atoxic (simple) goiters, both of which gave the same (9 per cent.) in the regenerating (D) class.

4. Twelve per cent. of the thyroids from the toxic non-exophthalmic cases of clinical group 2 are early fetal adenomas and 33 per cent. degenerating fetal adenomas, making 45 per cent. in all in which the pathology is that of encapsulated adenomas made up of acini of largely lumenless type. This leaves but 5 per cent. of the cases in clinical group 2 in which the pathology of the thyroid is that of colloid goiters, with adult parenchyma. This is in strong contrast to the distribution of the thyroids in the toxic cases from clinical group 1, in the positive ones of which only 7 per cent. of the thyroids are early fetal adenomas, 14 per cent.

[3] AMER. JOUR. MED. SCI., December, 1913, 781–90.

degenerating fetal adenomas (21 per cent. in all), while 62 per cent. of the thyroids in this clinical group 1 are colloid goiters with adult parenchyma. This distribution is closely followed by the thyroids in the questionable toxic group—E, 10 per cent.; F, 18 per cent.; G, 19 per cent.; H, 44 per cent. respectively—which also is almost parallel with the distribution of the thyroids from the non-toxic (simple) goiters—E, 5 per cent.; F, 18 per cent.; G, 23 per cent.; H, 44 per cent. This may all be summarized by saying that one-half of the thyroids from the toxic non-exophthalmic cases which more closely resemble true exophthalmic goiter (clinical group 2) are of the regenerative type, and nearly all the remainder are fetal adenomas, while, in contrast to this, only one-eighth of the thyroids from the toxic non-exophthalmic cases which do not resemble true exophthalmics (clinical group 1) are of the regenerative type, less than one-fourth are fetal adenomas and more than three-fifths of them are adenomas or colloid adenomatoses, with adult and atrophying parenchyma.

Average Age Distribution. Plummer has shown that patients with true exophthalmic goiter first notice the excessive development of the thyroid at an average age of 32 years, with evidence of intoxication developing 0.9 of a year later. The average age of these patients at the time of the removal of the thyroid was 25 years, in those cases in which the parenchyma of the thyroid was found to be in an early stage of primary hypertrophy and hyperplasia (pathologic group A), 31.7 years in those cases in which it was in an advanced stage of primary parenchymatous hypertrophy and hyperplasia (pathologic group B), 40.7 years in those cases in which it showed regressive changes secondary to primary hypertrophy and hyperplasia of the parenchyma (pathologic group C), or an average of 35.8 years for all cases in the group. The average age of the patients in clinical group 2 of the toxic goiter cases is lowest in those whose thyroids were of the regenerative type and highest in those whose thyroids were colloid goiters with adenomas or adenomatosis. This same is true throughout the other two groups of toxic goiters. It is worthy of note that the average age of the patients with toxic symptoms in both clinical groups is considerably higher than the average age of the patients with non-toxic symptoms in each of the pathologic groups. This is capable of several interpretations, the more obvious of which are (*a*) regenerations of atrophic epithelium (group D) require considerable time for the development of symptoms; (*b*) fetal adenomas on the average require more time for the development, if ever, of toxic symptoms than do regenerations; (*c*) adult adenomas and diffuse adenomatoses are slowest of all types to develop, if ever, toxic symptoms. In general, it may be said that patients with non-expohthalmic goiters either come to operation before they have

developed their toxic symptoms at an average age of from thirty-one to forty years acording to their pathologic classification, while patients with toxic non-exophthalmic goiters come to operation at an average age of from thirty-two to fifty-two years, according to their pathologic grouping. It is important, however, to control our deductions from a study of the average ages at operation by a consideration of the date of the next classification.

Average Duration of Goiter before Operation. The average duration of goiter before operation in the cases of true exophthalmic goiter is 0.3 year for those in which the thyroid was of pathologic group A (early primary parenchymatous hypertrophy and hyperplasia), 0.9 of a year in those of pathologic group B (advanced primary parenchymatous hypertrophy and hyperplasia) and 3.5 years in those of pathologic group C (regressing primary parenchymatous hypertrophy and hyperplasia). In the toxic cases of clinical group 2 the goiter had existed 6.9 years in those of pathologic group D (regenerations), 4.4 years in those of pathologic group E (early fetal adenomas) 12.6 years in those of pathologic group F (degenerating fetal adenomas), or an average of 8.8 years of the total fetal adenomas—and 14 years in those in which the thyroids were of pathologic groups G and H (colloid goiters with adult parenchyma). When the first of these figures are compared with the average duration of the goiters in the other groups, it would appear that those cases in clinical group 2 (*i. e.*, toxic goiters resembling exophthalmics) though they develop later in life, as shown by the average ages at operation, yet are of sufficient intensity to bring the patients to operation considerably earlier than patients of clinical group 1 or those of the atoxic group.

Average Weight of Portion of Gland Removed. The average weight of the portion of gland removed is in general a fair relative index of the total size of the thyroid. The examination of the average of these weights for thyroids in the different groups shows that of those from cases of exophthalmic goiter, those in pathologic group A (early primary parenchymatous hypertrophy and hyperplasia) are the smallest, 38 grams, those of pathologic group B (advanced primary parenchymatous hypertrophy and hyperplasia) are considerably larger, 61 grams, and that those of pathologic group C (regressing primary parenchymatous hypertrophy and hyperplasia) are smaller than the preceding, 51 grams. In those from clinical group 2 (toxic non-exophthalmics), those of groups D and E are much smaller than those of any of the other groups, 67 and 68 grams respectively. This observation is in harmony with the conclusions to be drawn from the average durations of goiter since these relatively smaller glands are those not so much blocked with retained colloid as are the thyroids of the simple goiter type. Indeed, throughout this clinical group 2, the average weight of

the glands of each of the pathologic groups is very much smaller than the average weight of the glands in parallel pathologic groups of either clinical group 1 or of those of the simple goiters.

General Summary. 1. The pathology of the thyroid in true exophthalmic goiter is essentially a primary parenchymatous hypertrophy and hyperplasia, *i. e.*, an increased amount of functionating parenchyma associated with an increased absorption. The process is an acute one.

2. The pathology of atoxic simple goiter is marked essentially by atrophic parenchyma, decreased function and decreased absorption. The process is a chronic one.

3. The pathology of toxic non-exophthalmic goiter of clinical group 2 (*i. e.*, those resembling exophthalmic goiter) is one of increased parenchyma through regenerative processes in atrophic parenchyma or the formation of new parenchyma of the fetal type, with an increase in each instance of secretory activity and of absorption. The process is a chronic one, but sufficiently active to cause the patient to consult a surgeon earlier than do those patients in clinical group 1.

4. The nearer the cases of clinical group 2 (toxic non-exophthalmics) approach, in age and symptoms, true exophhthalmic goiter, the shorter the duration of the period of goiter before operation and the smaller the average weight of the gland at the time of its removal.

5. The cases of toxic goiter of clinical group 1 (*i. e.*, those in which the symptoms are of the cardiovascular variety) much more closely resemble cases of simple goiter in their pathology in all respects than do the cases of clinical group 2. A larger number of them are of the colloid goiter type, the enlargement of the thyroid has existed for a longer period before operation, and the portion of the gland removed is materially larger than in those cases of clinical group 2.

6. Finally, it may be stated that all the above pathologic evidence points to a constant relative association of increased secretion and increased absorption from the thyroid proportional to the degree of toxicity on the part of the patient. We have as yet no absolute proof that such secretion and absorption is the cause of, rather than coördinate with, the symptoms, but the presented evidence strongly points to that conclusion.

THE STUDY OF RENAL FUNCTION: THE PROGNOSTIC VALUE OF STUDIES OF RENAL FUNCTION.[1]

By L. G. Rowntree, M.D.,

ASSOCIATE PROFESSOR OF EXPERIMENTAL THERAPEUTICS, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND.

Despite the increased light shed upon medicine generally by science, the aphorism of Hippocrates holds true today, "experience is fallacious and judgment difficult." Constant daily contact with nephritis in ward rounds, interspersed with occasional visits to the pathologist, serves to convert such an opinion into a conviction. Even the best clinical training and experience do not fully equip the physician to cope successfully and authoritatively with the problem of prognosis in certain cases of nephritis, nor do they reveal the exact status of his patient in many other pathological conditions of the kidney. To his assistance then are lately brought renal functional tests.

The ultimate object of any line of work is often furthered by a temporary abandonment of the consideration of details concerned in its various phases, and the replacement of this by reflection upon it in its entirety and in its relationship to its environment. A comprehensive review of any field of research, particularly in regard to its relationship to the fundamental sciences involved, and in regard to the absolute advancement resulting from it, is seldom amiss, since it often results in the disclosure of the uselessness and limitation of certain procedures, suggests new and better methods of attack, and establishes a truer conception of the purport and importance of the work.

The development and introduction of numerous renal functional tests are in accord with the general trend of medicine of today, the importance of knowing the ability of any organ to carry on its work, rather than the appearance of the cells engaged in the work, being even more emphasized.

Determination of renal function is of vital interest alike to the internist and surgeon from the standpoints of diagnosis, prognosis, and treatment. The widespread nature of the importance of such determinations is probably not so apparent to those confining their attention purely to its medical or surgical aspect, but to those interested in methods of determining renal functional capacity as such it becomes firmly impressed as investigations are made in relation to acute and chronic nephritis, orthostatic or other albuminurias, arteriosclerosis, uremia, myocardial insufficiency, polycystic kidneys, obstruction in the lower urinary tract, cystitis,

[1] Part of a symposium on Renal Function at a meeting of the Congress of American Physicians and Surgeons held in Washington, D. C., May 6, 1913.

pyelitis, unilateral and bilateral hydronephrosis, pyonephrosis, pyelonephritis and ureteral renal calculi, hypernephromas, renal tuberculosis, and the numerous allied conditions calling for differential diagnoses.

The clinical diagnosis made in any individual case, before offering a prognosis certain problems must be investigated: (1) What pathological condition underlies the clinical picture? (2) Is the condition localized to the kidney or is any other system (cardio-vascular) involved or likely to be involved? (3) What is the functional capacity of the kidney? Is this permanent or temporary, and subject to change? (4) Is or is not the condition amenable to treatment? Only by attention to all these factors can anything approaching correct prognoses be attained.

Renal functional capacity is usually ascertained in one of two ways: (1) Tests of excretory capacity through the quantiative determinations of the excretion of various substances in the urine, dyes—methylene blue, indigo carmine, rosaniline, sulphonaphthalein, other chemicals—potassium iodide, lactose, salicylates, sodium chloride, urea, sugar following phloridzin, and the enzyme diastase. (2) Tests of retention through quantitative determination of the concentration of certain substances in the blood, ions through electrical conductivity, molecules through cryoscopy, urea, incoagulable nitrogen, and cholesterin.

The recent work of Folin and Denis indicates that the concentration of urea, 0.5 gm., and of total incoagulable nitrogen, 0.6 gm. per liter, heretofore considered normal, must no longer be so considered, since in sixteen strictly normal individuals the highest non-proteid nitrogen which they found was 26 mg. and urea nitrogen 13 mg. per 100 gm. blood. Slight nitrogen retention may apparently occur in many diseases, but in our experience, with a large number of cases, using the older methods and also Marshall's new urea method, we feel that no great prognostic significance is to be attached to urea concentrations less than 0.55 and total incoagable nitrogen 0.5 gm. per liter. Greater concentrations than this, together with a serum freezing-point lower than −60°, are of the greatest prognostic importance. Evidences of retention reaching this degree we refer to as cumulative phenomena.[2]

These test all prove of value prognostically, but some much more so than others. Those of most importance in Group I are the dye substances, especially the phthalein, and of Group II, cryoscopy, total incoagulable nitrogen, and urea. The phthalein test is of prognostic value in all pathological conditions, whereas

[2] One would expect the urea and total incoagulable nitrogen in the blood to be approximately inversely proportional to the excretory efficiency of the kidney since this is the only channel of elimination (practically speaking) for the nitrogenous waste products.

certain cases of severe nephritis even in uremia show no marked increase in incoagulable nitrogen or urea. So the presence of cumulative phenomena is of the greatest prognostic significance, while their absence is not.

Functional studies reveal only the excretory capacity of the kidney. By themselves they do not make the diagnosis or settle the prognosis. Just as routine blood examinations occasionally reveal an unsuspected leukemia, the routine use of functional tests brings latent kidney involvement to light. These tests should be used routinely in conjunction with other procedures to aid in diagnosis, prognosis, and selection of lines of treatment. Their importance in different cases varies. It is possible that a series of ten or twelve different tests may add little or nothing to our knowledge of the condition after a careful clinical study, whereas after equally as careful a clinical study one test, verified, may change all of our ideas concerning the diagnosis, prognosis, and treatment; as for instance in one of our cases where a boy, prior to functional studies, was considered the subject of a diabetes insipidus, with an excellent immediate prognosis, and after one phthalein test was recognized as a case of advanced chronic interstitial nephritis verging on uremia, which was substantiated at autospy within two weeks. Because of our inability to determine in advance in what cases the functional studies will be of value, their routine employment becomes of paramount importance.

Clinical or functional studies alone are inadequate from the standpoint of prognosis. The application at any one time of one or a series of functional tests reveals only a limited amount of information, *e. g.*, the excretory power of the kidney at that particular time. This, apart from other considerations, may be of no great prognostic significance. In order to become so the data from such studies must be considered in conjunction with a careful clinical study, and the underlying pathological processes responsible for the clinical and functional pictures must be recognized, identified, and understood.

Aside from or in the absence of clinical studies, repeated functional estimations, with the employment of the appropriate test over a varying period of time, will reveal the nature (stationary, progressive, retrogressive) and degree of renal involvement, and so prove of prognostic value. But even repeated functional studies prove of greatest value when associated with careful clinical studies, for it has been definitely established that functional pictures carry different significance in various pathological (clinical and experimental) associations. Diseases may be functionally identical, clinically and prognostically different, and *vice versa*. To illustrate, a low condition of function, as indicated by a low phthalein output, together with marked delay in the excretion of chlorides, iodide, and lactose, may be encountered in experimental

chromium nephroses or in marked passive congestion (experimental or clinical). This may be followed within a week by a practically normal renal function owing to regenerative processes in the first instance and to the reëstablishing of cardiac compensation and better circulation in the second, whereas findings identical with those originally encountered, occurring in a case of chronic interstitial nephritis, indicate impending uremia and a grave prognosis. Again, identically low functional capacity in cases of urinary retention associated with pyelonephritis and hydronephrosis on the one hand, and in chronic nephritis on the other, do not have the same prognostic significance, since the surgical condition is amenable to treatment, whereas no efficient therapy is at hand in chronic nephritis. From this the necessity of understanding the absolute significance to be attached to the findings of any functional test becomes apparent. Lepine has objected to the employment of any one substance for the purpose of estimating functional capacity of the kidney, on the ground that the kidney does not excrete all substances with the same facility, and that data obtained from a study of the excretion of one substance, therefore, cannot be applied to others. He believes that each substance has its own coefficient of excretion. That there is not accurate and exact parallelism of excretion of all substances by the kidney, one is forced to admit, but that there does exist a certain degree of parallelism, the same general tendency of excretion for all of the substances so far used, is unquestionably true. The difference is one of degree. *Familiarity with the meaning of these variations in degree, to which peculiar prognostic significance attaches, is most desirable therefore.*

The value of any of these excretory tests is purely empiric, because of lack of sound physiological information dealing with the ultimate physics and chemistry of the excretion of any substance by any part of the kidney tubules or glomeruli. Experience has taught us that the failure of phthalein to appear in the urine or its excretion in mere traces in the course of chronic nephritis indicates impending uremia and grave prognosis, even in the absence of any definite knowledge concerning the excretion of any other substance. In other words, failure to excrete phthalein empirically signifies incapacity on the part of the kidney to carry on its work, hence a bad prognosis. But this does not hold for all substances. Failure to detect diastase in urine by the customary technique employed means renal injury, possibly severe renal injury, but not necessarily so.

How can we utilize functional tests to the greatest advantage prognostically?

1. The prognostic value of functional studies must be considered from two points of view: (*a*) As to the immediate outcome (days, weeks, or months are here concerned); (*b*) as to the ultimate fate

of the patient and the future course of the pathological processes. At present their value from the first point of view is definitely established, and is here discussed in its various phases. Prognostic significance other than immediate will be revealed only in the course of years. In association with Dr. Thayer and Dr. Baetjer an attempt is being made to learn of the condition through correspondence and reëxamination where possible of all of our patients previously studied. Data sufficient for conclusions are not yet at hand. Surgically, little prognostic value other than immediate, can be considered, since surgical interference so radially changes the condition.

2. We need a much greater familiarity with the significance and reliability of the findings of all these tests in all renal lesions, experimental and clinical, medical and surgical.

3. We must learn the relative ease with which each and every approved test responds to increasing degrees of injury of any type, such information as has been presented in experimental nephroses by Schlayer and his co-workers, by Pearce, Austin, and Eisenbrey, or in chronic passive congestion in more recent studies.

4. Experimentation and clinical experience must teach us upon which tests reliance as to prognosis can be placed in each and every type of renal disease.

5. We need a much deeper insight into the nature of the processes at work in certain diseases, *e. g.*, eclampsia, kidney of pregnancy, certain types of nephritis, etc. We must learn whether certain symptoms, conditions, and phenomena are actually due to the accumulation of toxins, ferments, etc., whether this accumulation does result from the failure on the part of the kidney to excrete them, or whether the kidney is the usual channel of their excretion. May not, for instance, certain of these phenomena be the expression of deprivation of the body of certain substances through excessive excretion through hyperpermeability? More light is needed on the factors responsible for hypertension, edema, uremia, etc. *We must learn to recognize in what conditions the excretory power of the kidney is a real criterion to the patient's actual condition.* Prognostically their value will thus be enhanced through a knowledge of the limitations of these tests.

6. Functional tests will become more generally used, and hence of more value when we know which ones can be discarded without loss and which combination of tests (the smaller, the better) will yield all the information necessary in any given type of disease.

Value in Medical Cases. Until recently little or no prognostic value has been attached to functional studies in medical cases, although their worth in this connection is fully as great as in the surgical. The introduction of new tests, notably the phthalein, and improvements in the technique relating to the old ones are largely responsible for the change in the attitude of the

profession. The limitations of the value of such tests must be clearly recognized. In all forms of renal disease a prognosis only so far as renal efficiency or inefficiency can be made through their use. Death may occur from innumerable other factors, concerning which they give no information.

In *acute nephritis* the prognosis is largely dependent upon the etiology. When associated with specific fevers it become impossible to ascertain whether the patient is suffering from a toxemia due to non-excretion or one due to a specific toxin of the fever. The capacity of the kidney to excrete can be readily determined, but this means but little prognostically on account of the rapidity with which marked changes in this respect occur. Clinically we have seen cases without 10 per cent. phthalein output for two hours excrete 28 per cent. four days later and the normal amount within two weeks. Experimentally, chromium animals with a zero output for two hours have returned to a normal excretion within ten days, while twenty-four hours later, more chromium having been given, the phthalein was again not excreted. It is evident, therefore, that frequent repetitions of tests are essential to prognosis in acute nephritis. But when a patient exhibits, as one of ours did, no phthalein, no lactose, together with a high blood urea concentration, the case must be considered a grave one, though not hopeless. The immediate danger from the renal inadequacy factor is at least determined.

The functionally mild nature of a *chronic nephritis* is readily recognized. Associated with the albumin and casts, a slight increase in blood pressure, palpable vessels (arteriosclerosis?) and slight cardiac hypertrophy, there may be encountered a somewhat delayed lactose and phthalein excretion, a normal total salt output, with a vascular hyposthenuria, but no evidence of cumulative phenomena. In such a condition the immediate outlook is favorable, but tests should be applied intermittently to determine whether the condition is stationary or progressive and the rate of progression. In prognoses caution should be observed on account of the possibility of acute exacerbations becoming superimposed on the chronic process. Aside from this the case may develop gradually into an advanced nephritis, with marked renal insufficiency exhibiting uremia, into a nephritis with a cardiac insufficiency or with a vascular accident (apoplexy).

Advanced nephritis is indicated always by decreased excretory capacity and usually by cumulative phenomena. Although clinically it is difficult often to determine the severity of the condition, this is readily obtained through functional studies. Perhaps the majority of cases of chronic interstitial nephritis are clinically latent, unrecognized until the occurrence of serious or even fatal complications. Uremia clinically may appear to come out of a clear sky, whereas its unsuspected proximity can be readily recog-

nized and its occurrence can be easily predicted through functional studies. In chronic nephritis, failure on the part of the kidney to excrete phthalein or lactose, together with marked cumulative phenomena, indicates renal insufficiency, impending uremia, and calls for a grave prognosis.

Other cases with marked clinical nephritis, even with mild uremia, but with less marked functional involvement, may be more difficult for prognosis. Many factors must be considered. Will the heart dilate? Will an apoplexy occur? Will an acute attack be superimposed? But so long as the renal function remains fair, say 30 per cent. phthalein for two hours, with cumulative phenomena absent, and none of the above complications arise, death from renal insufficiency, uremia, is not at all likely, and an immediate favorable prognosis can be given. Care must be used in predicting more than this. The tests should be repeated in order to follow the course of the disease.

That a good or normal phthalein output is occasionally encountered in the presence of definite nephritis has been pointed out in our earlier publications. At the same time the absence of hyperpermeability to phthalein in all our studies was commented upon. Pepper and Austin have lately called attention to a case of nephritis with marked albuminuria, cylindruria, and edema in which the phthalein and total incoagulable nitrogen were normal, while the chloride output after additional salt was somewhat delayed. The phthalein output in this case, 67 per cent. for one hour, strongly suggests hyperpermeability. Baetjer in our clinic has encountered four cases during the winter which clinically and functionally resemble Pepper and Austin's case, and in all of which hyperpermeability to phthalein and lactose was strongly suggested. This type of nephritis is not well understood. Since all of the patients studied are still living, the nature and extent of the anatomical lesions are as yet undetermined, and the value or significance of functional studies in relation to them is not clear. Since the patients have continued to live, the tests furnished correct information so far as immediate prognosis at least is concerned.[3]

Cardiorenal Cases. All grades of nephritis and myocardial insufficiency may be associated, and only through the use of clinical and functional studies can the cases be properly interpreted. By the combined studies it is possible in any given case to determine the relative responsibility of the kidney and heart from the clinical picture presented, and thereby to arrive at a better prognosis.

Experimentally it has been shown that in moderate degrees

[3] It is possible that this increased permeability is not a passive condition but an active functional response to some unknown renal stimulant, which differs essentially from an ordinary diuretic.

of passive congestion the excretion of lactose, iodide, and salt may be delayed, while the phthalein output remains normal. When the congestion is more severe the phthalein is decreased, but returns to normal with the earliest signs of improvement of circulation. Strauss and Hohlweg found that incoagulable nitrogen and urea of the blood are increased in chronic passive congestion, but not so strikingly as in nephritis, findings which we are able to corroborate. Low phthalein and the cumulative phenomena, therefore, bear great prognostic and diagnostic significance in this group of cases, since they are only encountered with rather advanced nephritis or with a severe passive congestion calling for a grave prognosis.[4]

Moderately advanced nephritis associated with a moderate myocardial insufficiency often exhibits a fair renal capacity, in which case the prognosis rests more on the response of the heart to treatment than on the nephritis. An increase in the phthalein output may be the first evidence of restoration of cardiac compensation, and hence it indicates a favorable immediate prognosis. The absence of cumulative phenomena, together with a fair phthalein output in any clinically severe cardiorenal disease, points to the heart as the responsible factor.

A low excretory capacity, with marked increase in blood urea or total incoagulable nitrogen or a low serum freezing-point, indicates either that the kidneys chiefly must be considered etiologically or that the heart is in an extremely precarious condition; in either case the prognosis is grave. With or without cumulative phenomena a low excretory capacity persisting after clinical evidence of cardiac improvement indicates severe nephritis and an unfavorable prognosis.

Myocardial Insufficiency. Marked renal insufficiency may result from pure chronic passive congestion. Exceptionally, clinically and experimentally, the functional studies reveal a decrease in function equaling that seen in the severe grades of nephritis. Since the congestion for this must be of a most extreme grade, death is imminent on account of the heart. As a rule in myocardial insufficiency, with a symptomatic and urinary picture identical with that seen in a moderately advanced nephritis alone or in nephritis associated with a cardiac break, renal function as indicated by both excretory and retention tests is surprisingly good. When low renal function is followed by an increased phthalein output the amount of increase gives a fair approximation of the extent of cardiac improvement.

Polycystic Kidneys. All conditions of renal function may be here encountered and a prognosis can be based upon functional

[4] In pure chronic passive congestion we have never seen the rest nitrogen higher than 0.63 gm. per liter.

findings in this condition just as in chronic interstitial nephritis. A case has been reported exhibiting a normal function, death resulting from an intercurrent disease, while a zero phthalein was found by Pepper and Austin in a case dying in uremia. A case now under observation, the diagnosis being confirmed by collargol skiagram, has a fair function only, 20 per cent. phthalein for two hours.

Surgical Cases. Uremia after operation has been responsible for a large proportion of the mortality in renal surgical cases, so that any method capable of furnishing information as to the probability of the occurrence of such a condition is of great importance to the surgeon.

Emphasis upon one point is needed, viz., a fair or a normal renal function must not be interpreted as meaning that uremia or anuria will absolutely not develop after operation, or as meaning that the postoperative function will be the same as that before surgical interference. Many accidents may occur. The subject of a perfectly normal function may, after operation, develop anuria and die, although other things being equal he is much less apt to do so than a patient who prior to operation has a low renal capacity. The great value of these studies surgically lies in their ability to reveal those cases which are suitable and those which are unsuitable for operation so far as the kidneys are concerned. They indicate that uremia is certain to occur following operation in a given case, that certain cases are hopeless, others poor, good, or excellent surgical risks, but they offer no absolute security that the subject of a good surgical risk will not develop renal insufficiency.

The previous knowledge of the renal function is also of prognostic importance in the event of development of postoperative uremia, for the occurrence of this condition in one who has been previously shown to have a continuously low function means a grave prognosis, whereas in one who has had a good renal function recovery is more probable.

The tests are of value in two classes of cases: (1) Those with retention of urine, renal injury following, due to obstruction in lower urinary tract, with back pressure upon the kidney resulting in functional changes, in hydronephrosis, or in pyelonephritis, etc., and (2) those with unilateral or bilateral renal disease.

Obstruction in Lower Urinary Tract. As a result of obstruction in the lower urinary tract, pathological changes may occur in the ureter and kidneys, dilatation of the ureters, varying grades of hydronephrosis, and, as a result of the long-continued high pressure, atrophy of the parenchyma of the kidney. Not infrequently infection occurs with the development of a pyelitis, a diffuse or localized pyelonephritis, or pyonephrosis. The occurrence of these complications is often difficult of recognition, and is often overlooked, especially in the absence of symptoms of

renal inadequacy. Cystitis and associated albuminuria and cylindruria are usually present, albumin and casts not contra-indicating operation. The urinary output may be normal in many instances, also the urea output and total solids, and yet the patient be on the verge of renal failure. Diastrous results may be certain to follow any radical surgical intervention at this time, yet often nothing outside of functional studies can furnish this information.

A marked decrease in the excretory phenomena alone or associated with cumulative phenomena means severe derangement of renal function which may be of either a temporary or permanent character. No prognosis should be given, and, except in emergency or where the surgical procedure employed is the only method of improving or relieving the renal disturbance present, no surgical interference attempted without further study in conjunction with suitable preliminary treatment (Young's treatment, catheter drainage, and abundance of water). Under this regimen repeated tests will quickly demonstrate the nature of the derangement, cases of nephritis and of true interstitial destruction showing no improvement, whereas purely functional changes or those secondary to pyelonephritis show markedly increased function.

This constitutes a striking group of cases. A patient in uremia, with low excretory functional findings and with cumulative phenomena, may in the course of a few weeks return to an excellent clinical condition, with a renal functional capacity approaching normal. Only one such experience is necessary in order to impress upon physician and surgeon the importance of determining (through time, preliminary treatment, and repetition of tests) the nature of the depressed function, temporary or permanent. The prognosis of the operation, so far as uremia and anuria are concerned, is infinitely better in those cases showing marked improvement in renal function following the adoption of the preliminary treatment above mentioned.

All tests are not of equal prognostic value in this group of cases. The phthalein had already established its place. Lactose is of no significance, since its total suppression is frequently encountered when the phthalein, diastase, cryoscopy, blood nitrogen, and urea all show a fair or moderately good renal function, the truth of which is demonstrated in the subsequent history. In a series of twenty such cases, lactose was recovered in the urine in only six instances. Glycosuria following phloridzin is also slow in appearance or fails to appear at all. These two tests, therefore, exaggerate the degree of functional changes and bear no prognostic significance.

The phthalein test along with cryoscopy, urea, and non-proteid nitrogen determinations of the blood, gives a sharp index of the functional capacity.

UNILATERAL AND BILATERAL SURGICAL DISEASES. The prognosis in unilateral and bilateral surgical diseases of the kidneys depends upon the surgeon's ability to recognize prior to nephrectomy which is the diseased or more diseased kidney, and what is the functional capacity of the kidney that is to be left to carry on renal function, as well as upon his technical skill and the nature of the pathological process present. Tuberculous and pyogenic infections, unilateral and bilateral calculi, hydronephrosis, hypernephromas, and congenitally deficient or non-developed kidneys are the conditions in which the tests have proved of most value.

The urea, indigo carmine, methylene blue and diastase, cryoscopy, phloridzin, Alberran's polyuria tests, along with clinical studies and urinalysis of the separated urines, will all indicate which is the diseased or more diseased kidney. But in this class of cases the shortcomings of most of these tests are evident, since one kidney may be doing two or three times as much work as the opposite one and yet be incapable of assuming the additional work or of carrying on adequate work unaided. It may be doing the major part of the work, but only at the expense of its reserve power. But phthalein has prognostically one great advantage over other functional tests, in that it indicates the absolute as well as the relative value of each kidney, so that one knows not only which is the diseased or more diseased kidney, but the amount of work each is doing relative to the other, and what is yet of greater importance the amount of work for each relative to the normal, since this allows a prognosis concerning the capacity of the remaining kidney to carry on renal function. In double renal tuberculosis, in which for instance the amount of pus from each side is practically the same,[5] the phthalein test may demonstrate that one kidney has a function far in excess of the other—in fact, so good a function that a successful nephrectomy can be done.

It must be admitted that depressed function, the result of inhibition due to ureteral catheterization, is sometimes encountered, in fact more frequently than we formerly believed. But in every case demanding ureteral catherterization a total renal determination should also be made through which any discrepancy can be readily detected and error be thereby avoided. Where leakage inhibition occurs reliance is placed upon urea percentage and diastase.

Of prognostic significance also is the development of increased functional capacity in the remaining kidney after a nephrectomy. In those cases in which determination of function has been made after an interval of a month after operation the capacity has not only been greater than that of the same kidney, but equal to or greater than that of the combined function of the two kidneys

[5] Not infrequently in bilateral renal tuberculosis the more recently involved kidney secretes more pus than the other and only through functional tests can the true condition be recognized.

PROPERTY OF
ATLANTA MEDICAL COLLEGE

prior to surgical interference. The amount of increased function that will develop can of course not be predicted from functional studies, but the increase after nephrectomy can be determined from day to day and so aid in prognosis.

A perfectly normal urine in every respect except quantity may be excreted by a congenitally deficient type of kidney. Such a kidney may be capable of doing only one-fifth to one-tenth of the total work required. The literature furnishes numbers of instances of death following a nephrectomy owing to the presence of this unrecognized deficient kidney which has been left to do all the work. In the last four years in our experience four such cases have been encountered, and in the last case only the presence of a low phthalein from this kidney revealed its true nature and prevented the removal on the opposite side of a tuberculous kidney which had many times a greater function than this supposedly healthy kidney. Had the nephrectomy been performed the prognosis would have been extremely grave.

In certain cases, owing to malformation or stricture in the lower end of the ureters, and especially in bladder tuberculosis, it may be possible only to catheterize one ureter. When infection of the bladder exists, microscopic and chemical examination of the urine collected transvesically is obviously unreliable as indicating a healthy or diseased condition of the uncatheterized side. It is therefore necessary to use functional tests to determine the presence or absence of disease and the extent of the disease where it does exist. A prognosis may be safely made concerning the ability of any kidney to carry on the renal function alone even when catheterization of the ureter is impossible and where the urine has been collected through a diseased infected bladder, provided a catheter can be inserted into the other ureter.

The use of these tests should not be limited to renal surgery, since their routine employment would undoubtedly influence the surgeon's attitude in many instances.

Uremia. Uremia is a clinical condition, a syndrome ill-defined, resulting from renal insufficiency from any cause. Its appearance is often sudden and unexpected, and its course is acute and severe, rapidly ending in death, or chronic, lasting through months. Through functional studies it is possible to ascertain that it is impending even when no indications whatever of its proximity are revealed by the clinical study. With a continued failure on the part of the kidney to excrete phthalein and lactose, etc., associated with the continuous marked and increasing accumulation of urea or total incoagulable nitrogen or low serum freezing-point, one is perfectly safe in predicting the early appearance of uremia regardless of the underlying pathological condition.

Uremia once present the clinical severity is not a safe criterion for prognosis. Apparently desperate conditions sometimes reveal

a fairly good renal function with an ultimate recovery, whereas very mild symptoms may be present until shortly before death. It always, however, indicates a serious condition, always calls for immediate therapeutic consideration, and always suggests a grave prognosis, but it does not always indicate a hopeless one.

It has already been intimated that identical functional pictures carry very different prognostic significance in different clinical and pathological associations. Extremely low functional capacity in chronic nephritis means death, whereas in obstruction in the lower urinary tract with urinary retention and back pressure the injury may be mostly functional, so that following appropriate treatment a fair or good capacity is again established. Nothing is more surprising than the rapidity and extent of the functional and clinical improvement. Whenever renal function markedly increases, surgical interference is much less liable to be followed by postoperative uremia, whereas in practically all cases with persistent low function it has followed operation used as a last resort, and death has ensued.

Markedly different clinical and functional conditions are encountered even in medical uremia. Some cases of mild uremia, with nausea, vomiting, and even stupor, show a phthalein output which is relatively high, 20 to 35 per cent. for two hours. This type is much more apt to be associated with cardiac or vascular changes, with edema frequently a prominent feature. The uremia symptoms may here be an expression of a different pathological condition than that encountered at other times, *e. g.*, edema of brain rather than a pure toxemia. These cases often improve and leave the hospital; if death supervenes, it is usually a cardiovascular affair and not a typical uremia.

Occasionally, with low excretory function (traces of phthalein) and marked cumulative phenomena, the patient will continue to live in a chronic uremia for a surprisingly long time. In several instances such a patient has lived for some months, and in one instance the patient lived a year. This patient is in a desperate condition but still continues to live with 20 per cent. phthalin for two hours and with a blood urea 2.5 gm. per hour. Vicarious activity probably varies markedly in different individuals, and though incapable of carrying on life alone for any length of time, it probably is a material aid in the maintenance of life when the kidneys are just verging on inadequacy. The balance is not long maintained, however, and death is continually imminent.

Uremia cannot occur without valuable evidence appearing as decreased excretory phenomena, but cumulative phenomena do not always arise. With Hohlweg we consider increased blood urea and rest-nitrogen indications of renal insufficiency and not of uremia.

THE PROGNOSTIC VALUE OF EACH TEST. The employment of one test alone does not always yield all the information desirable. When only one is used the phthalein test is undoubtedly the one of choice. When it reveals decreased renal capacity, one of the blood tests, urea, total incoagulable nitrogen, or cryoscopy, should be employed to determine the presence or absence of cumulative phenomena. These probably carry about the same significance.

Dye substances other than phthalein need not be employed prognostically, since they yield less quantitative and less reliable results and add nothing to prognosis.

The phthalein is the test for general use under all conditions. Its findings can be verified and its indications strengthened by the employment of selected tests in different conditions.

The iodide and salicylate tests are not of great prognostic value.

Lactose is unreliable, since its total suppresion occurs in moderate lesions of a given type, but suppression in chronic nephritis indicates a severe lesion.

The urinary urea is of value only in relation to unilateral renal disease.

Phloridzin has a tendency to exaggerate the degree of functional injury, and hence is not of great value.

Salt. A marked tubular hyposthenuria carries much prognostic significance, otherwise the chlorides are of only slight prognostic value.

Water. A marked oliguria or anuria persisting is of significance.

Diastase may be tremendously depressed in moderate degrees of renal injury, in chronic passive congestion, while at other times it is not affected proportionate to the injury, hence it is not reliable for total capacity. In unilateral cases the diseased kidney is correctly indicated.

The value of total incoagulable nitrogen and of urea in the blood has been enhanced by the introduction of newer and more accurate methods by Folin and by Marshall. Increased concentration of these substances does not always occur in severe renal involvement, hence their normal concentration in the blood does not indicate normal kidneys. Their increase signifies renal injury, and the extent of the increase is of extreme value in determining the extent of the injury. They are not of value in determining the diseased kidney where only one is involved.

Cryoscopy occupies a similar position with about the same significance. A study of the combination of these three tests is needed in order to determine the extent of parallelism in their findings.

With cholesteremia we have had no experience, and with the Ambard-Constant not sufficient to justify an expression of an opinion.

IRON INFILTRATION IN THE FIXED AND WANDERING CELLS OF THE CENTRAL NERVOUS SYSTEM.

By D. J. McCarthy, M.D.,
PROFESSOR OF MEDICAL JURISPRUDENCE, UNIVERSITY OF PENNSYLVANIA.

In a contribution to (*a*) iron infiltration in ganglion cells and (*b*) forced movement due to cellular degeneration of the cerebellum following rattlesnake poisoning,[1] I pointed out the existence of iron infiltration in the cortical ganglion cells both as an end result and as an intermediate process of the absorption of hemoglobin. The ganglion cells gave the biochemical tests for hemosiderin. The microchemical reactions in the large pyramidal cells in the cortex were striking and characteristic. In the Weigert-hematoxylin method the entire cell with its processes took a deep black stain. In thin sections this pigmentation seemed to consist of fine black granules; these black granules could be followed into the dendrites and produced an appearance of fragmentation. With the slow eosin stain the ganglion cells gave the same brilliant red reaction as did the red-blood corpuscles. With the potassium ferrocyanide and alcohol differentiation, the ganglion cell as a whole gave a diffuse blue reaction without, however, the ganular arrangement of the hematoxylin stained cell. This microchemical reaction in the ganglion cells was not obtained throughout the entire cortex, but only in the neighborhood of the diseased vessels.

Weber[2] has described iron infiltration in the cortical ganglion cell with similar changes to those here noted, but no other contribution, so far as I have been able to determine, has been made to this subject. This condition must indeed be a rare one, as I have noted it, as a complete reaction, only in the case above noted, reported by me. It is not a constant reaction in hemorrhage into the cortical tissues. I have looked for it in a large number of brains showing cortical hemorrhage, with degeneration of the red cells in various stages, but have not been able to find it. In a series of experiments on young puppies an artificial thrombosis of the venous sinuses was produced in an attempt to simulate the venous capillary hemorrhage observed in some cases of the cerebral palsies of childhood. Capillary hemorrhages in the tissues were produced, but no end reaction of hemosiderin was noted. What might be considered an intermediate reaction was the rule. Cells took a deep black stain with hematoxylin and a deep red stain with eosin, but no blue reaction with potassium ferrocyanide was obtained. The results of this series of experiments were inconclusive in

[1] Contributions from the William Pepper Laboratory of Clinical Medicine, 1900, vol. i.
[2] Monats. f. Psychiat. u. Neurol., 1898, No. 3.

demonstrating a structural change in the ganglion cell as a result of long-standing venous stasis or thrombosis occurring at the time of delivery. The experiments have not yet been completed, but so far as they have been carried, an artificial infiltration of hemosiderin in the ganglion cells has not been produced. In line with this work a careful investigation of ganglion cells was made in the brain from a patient who suffered from an extensive hemorrhagic encephalitis in the cortex. The iron reaction was not demonstrated in the cortical ganglion cells in this case, but was obtained in a striking cell reaction in the plasma-like cells of the pia arachnoid and in the elastic coats of the smaller cortical arteries. The case was as follows:

The patient, R. L., a white male, was admitted to the hospital, June 1, 1910 in a semi-unconscious condition, in which he remained for four days. On admission his neck was rigid, his pupils contracted and his reflexes exaggerated, and since the stuporous condition had been present, any attempt to move his neck or bend his back caused him to cry out as if from pain. Pressure upon the muscles also caused him pain. He had incontinence since his admission. Owing to the noise he made during any attempt to examine his heart and lungs an accurate knowledge of their condition could not be ascertained. There was, however, apparently no valvular lesions of the heart. In the left lung many dry rales could be heard in front. The patient had an old, depressed fracture near the Rolandic area on the left side. There was a large discolored area over the right temporal region; and just below the left deltoid muscle, on the outer side of the arm, was a large bruise. He had been operated upon shortly before coming into the hospital for a tuberculous fistula in ano, which was still unhealed. His wife later stated that he had been operated upon for fracture of the skull in September, 1908, which explained the depression.

On June 25, an examination of the eyes showed the eye-grounds to be normal, though the optic nerves were very small. A lumbar puncture revealed nothing abnormal macroscopically or microscopically, but a Noguchi (Butyric acid) test was positive. The urine had a specific gravity of 1026, and contained a trace of albumin; the microscope revealed granular casts, triple phosphates, and amorphus urates. The temperature was normal except for a slight rise during the fortnight preceding his death. The patient died July 25.

The autopsy on July 26 permitted the following diagnosis: Dilatation of the left ventricle; fibroid myocarditis; congestion and edema of the lungs; an old fracture of the skull; a chronic internal hemorrhagic pachymeningitis. The general postmortem examination showed nothing more than the above diagnoses suggest. The man was fairly well-nourished; the lungs were free and crepitated throughout, but contained frothy bloody fluid, while the pleural

cavities were empty. The heart was flabby, with the muscle pale in color, but no lesion was found in the valves, and the coronary arteries were smooth. The papillary muscles were slightly fibroid at the tips, and the aorta showed a few yellowish patches. The liver contained an excess of blood, and the spleen was large and soft. The pancreas, adrenals, ureters, and bladder were normal. The kidneys showed no noteworthy change. There was no gross lesion of the intestines, but these with the stomach, which presented a dark reddish mucosa, were distended. In the abdominal aorta were a few calcareous patches.

The skull showed a fracture partly linear in type, extending from the right posterior fossa just behind the foramen diagonally across the median line to the left fossa, and running superiorly and anteriorly close to the juncture of the parietal and temporal bones and terminating anteriorly at the base of the skull, just posterior to the orbital plate of the frontal bone on the left side. There were two small circular deficiencies in the frontal bone of the left side near the median line.

The brain showed slight excess of fluid. The inner surface of the dura, over practically the entire hemisphere, but especially posteriorly and superiorly, was thickened and darkened in color. At points the thickening appeared to be due to fibrin. At other places it appeared to be newly formed tissue. Posteriorly the superior surface of the brain showed a distinct depression underneath the thickest portion of the dura. The cord presented no gross lesions.

The gross examination of the brain, after hardening, showed at the base an advanced grade of arteriosclerosis of all the vessels composing the circle of Willis. There was a slight trace of chronic leptomenigitis over the base of the frontal lobes, and there were evidently adhesions between this and the dura of the base, which were torn away when the brain was removed. There was a yellowish pigmentation of the pia arachnoid over the base of the frontal lobe on the left side and the tip of the left temporosphenoidal lobe. Pons and medulla were normal. There was an extensive hemorrhagic internal pachymeningitis involving the dura over the convexity of the left hemisphere. On this side of the brain the pia arachnoid was adherent to the dura over the anterior half of the frontal lobe. The pia arachnoid as far back as the midparietal area had a yellowish red appearance, as if infiltrated with an old transformed blood pigment. Here and there throughout the frontal lobe, and more particularly where the pia arachnoid was adherent to the dura, the cortex was friable and softened as if from a recent thrombotic lesion. Sections of the cortex showed that the reddish-yellow pigmentation extended into the gray corticle matter, while the underlying white matter had the appearance of yellow softening. The dura over the right hemisphere was the seat of a localized pachymeningitis (6 cm. long by 3 cm. broad) situated over the

inferior parietal area. The internal surface of the dura was perfectly normal, both in color and texture. The external surface of the dura was roughened, indurated, and of an orange-brown to black color. Section of this area showed this condition for the most part to be extradural. The pia arachnoid on the right side was normal in texture and color, as was also the cortex. Transverse section of the brain showed nothing abnormal.

Microscopic Examination of the Brain Cortex. The left cerebral cortex showed here and there throughout the frontal area capillary hemorrhages, both old and relatively recent. The cortex in sections taken from the frontal lobe showed necrotic areas extending from the surface into the subcortical tissue in the form of pyramids. At the apices of these pyramidal areas of degeneration there was proliferation or neuroglia, while the body of the pyramids was composed of partially degenerated cortical substance and partially organized cortical scar tissue. New-formed capillaries were scattered throughout this area, and here and there capillary hemorrhages were present. A large number of a vesicular type of cell, containing an orange-brown pigment, was scattered through the areas of degeneration.

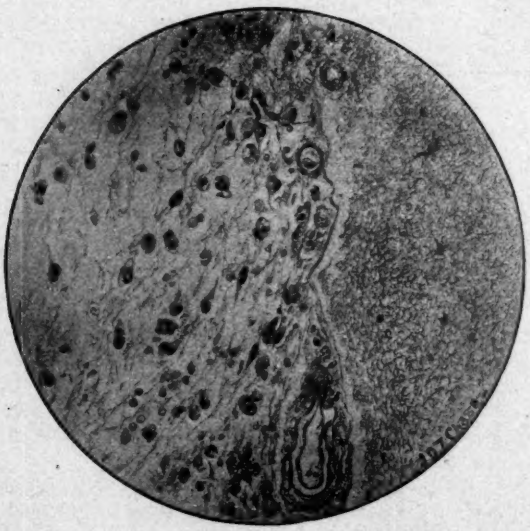
The dura mater over the left side of the brain was composed of laminæ of fibrous tissue, containing a great number of cells, mostly with connective-tissue nuclei, and containing pigment varying in color from light yellow to black. On the inner surface there was a layer of pseudomembrane, composed of trabeculæ of connective tissue, new-formed capillaries, and a great number of red-blood corpuscles. The connective-tissue cells contained yellow and black pigment.

Throughout the motor cortex on the left side there was a proliferation of neuroglia cells in the tangential and subtangential layers. The pyramidal cells showed a mild grade of chromatolysis, and appeared to be fewer in number than in the normal cortex. The left parietal and occipital areas were normal in structure. The cortical tissues of the right side revealed no abnormal change.

The pia arachnoid of the frontal and motor area of the left side showed a proliferation of the connective-tissue trabeculæ with an infiltration of red-blood cells, in various stages of degeneration into the interstices. Scattered through the arachnoidal spaces were found a great number of cells of a large vesicular type, filled with pigment varying in color from a light yellow to an orange-brown. The relative number of these cells in the sections depended upon the degrees of hemorrhagic infiltration in the meninges and neighboring tissues.

All the tissues showing this condition were stained for hemosiderin. The Berlin-blue reaction was not obtained in any of the cortical cells. A well-defined, clear-cut, blue reaction was obtained, however, in many of the vesicular type of cells in the pia arachnoid.

The elastic tissue in the small arteries of the pia arachnoid and superficial areas of the cortex took the same clear-cut, blue color as did the plasma cells above mentioned. None of the other tissues gave this reaction. Sections of the bloodvessels gave a microscopic picture, very much as that seen in the sections stained with a selective elastic stain. While the cortical ganglion cells did not give the stain reaction for hemosiderin in the sections stained with iron hematoxylin, both the neurogliar nuclei and the partially degenerated cortical ganglion cells in the neighborhood of the pyramidal areas of necrosis, gave a jet-black reaction, which I have already pointed out in a previous contribution to this subject may be considered as a partial or transitional stage between hemoglobin and hemosiderin.



Section through cortex and pia arachnoid. The small cells with hard granules gave the typical hemosiderin reaction. The small vessels also presented the Berlin-blue reaction.

Sections from the spinal cord showed a degeneration in the cross-pyramidal tract of the right side.

The area of external pachymenigitis on the right side was found, under the microscope, to be composed of (*a*) a normal dura somewhat thickened, and (*b*) external to this a thick layer composed of fibrous tissue, but relatively looser in consistence than that of the normal dura, containing a large number of connective-tissue nuclei and here and there large areas in which red-staining nuclei the size of red-blood corpuscles, but irregular shape, were found arranged in columns and nests. Connective-tissue nuclei and large

irregular cells scattered here and there contained masses of dark pigment having the appearance of melanin.

The biochemical microscopic reactions here noted threw some light on the minor changes in the nerve cells, leading to a disturbance of function, without apparent structural change. The partial reactions to iron infiltration shown in the ganglion cells, together with the complete reaction noted in the arachnoidal free cell, and in the coats of the capillary vessels were evidently only temporary in nature. These changes may entirely disappear, and studies of these tissues in after life would leave us without any evidence of these previous pathological lesions. In a complete stage of iron infiltration in the cortical ganglion cells, complete chromatolysis with disintegration of the cell occurs. In the minor grades of iron infiltration, relatively little structural change is noted in the cell. Granted such a transitory process, extensive disturbance of the function may result without leaving any changes evident in the histological picture. In cases of mental retardation, high-grade imbecility, etc., the brain structure not infrequently presents a normal histological picture. There is no reason, in this group of cases, why the functional activity of the brain cells should be subnormal. In conditions of prolonged passive congestion at birth, and more particularly in those cases where the microscopic examination of the newborn children, dying at or shortly after birth, reveals an osmotic extravasation of red-blood cells in the tissues, a medium grade of iron infiltration may well have taken place, leaving the brain structure normal, but with deficient functional power.

The meaning of the hemosiderin reaction in the elastic coats of the capillary vessels is not altogether clear, None of the other coats of the vessels gave this reaction. It is evidently a selective reaction, due to some changes in the elastic fibres. It was not present in the larger vessels within the area of blood extravasation and degenerating blood cells.

The extensive vascular changes noted in this case are of considerable interest from the standpoint of legal medicine. As a result of traumatism of the head, with a linear fracture, the following series of changes are presented: Extensive cerebral necrosis with hemorrhagic extravasation into the cortex on the side of the lesion, internal hemorrhagic pachymeningitis on the opposite side, together with an area of external hemorrhagic pachymeningitis on the posterior part of the dura on the side opposite to the bone lesion. There is a history of the excessive use of alcohol. How far are these changes due to the original trauma? It has been held by experts in court that concussion with a prolonged period of unconsciousness, without evidence of focal lesion or lesions, produces disturbances of the physical or nervous health of the individual, from which he practically never recovers. The lack of

resistance to stress and strain in such cases, a matter of clinical observation, not only in medicolegal cases but also in cases without a cause for legal action is probably due to relatively minor changes in the cerebrovascular system as compared to those here noted.

In the history of this case, it is shown that the patient apparently recovered from the cerebral injury after the operation. A succession of vascular accidents beginning with the cerebral injury and possibly influenced by the excessive use of alcohol took place, leading finally to his death. It is reasonable to suppose that these changes would not have taken place in the absence of any such injury. Certainly, the exact nature of the changes was determined by the extensive laceration of the brain tissue incidental to the original brain injury. Extravasating hemorrhage into the pia arachnoid is a relatively rare pathological phenomenon. I have seen it in one other case affecting approximately the same distribution in the brain in a case of locomotor ataxia.

The necrosis of the cortical and subcortical tissue is difficult to explain. It is possible that the inflammatory adhesions of the pia arachnoid to the dura produced partial or complete obstruction of the cortical capillary or both the capillary and the cortical venous circulation. The pyramidal shaped areas would be more in favor of a subcortical capillary destruction.

A PRACTICAL APPARATUS FOR THE PRODUCTION OF THERAPEUTIC PNEUMOTHORAX: WITH SOME NOTES ON THE MODUS OPERANDI, INDICATIONS, AND CONTRA-INDICATIONS.[1]

By S. Adolphus Knopf, M.D.,

Professor of Medicine, Department of Phthisiotherapy, at the New York Post-Graduate Medical School and Hospital, New York.

In presenting this new apparatus, originally the Forlanini apparatus, which was modified by Saugman, again by Muralt and Nebel, and then upon my suggestion made by the Kny-Scheerer Company in a little more substantial form, more easy to transport, more clearly graduated, and with glass tubes inserted in the rubber hose connecting the apparatus with the thoracic cavity, I do not wish to claim any credit for bringing out what I believe to be a very superior apparatus. The credit is due to the original inventors, Professors Forlanini and Saugman, and also to the Kny-Scheerer Company, who, as above stated, have made the apparatus compact, safe, and transportable.

[1] Read by invitation before the meeting of the Association of Physicians attending the Tuberculosis Clinics of New York City, October 8, 1913.

Those who have had experience heretofore with the Forlanini apparatus now on the market, will appreciate the difference. Shipped from a distance, the apparatus usually arrived with the glass tube broken and the gas containers unsupported, and if not broken, liable to break at the slightest jar.

Among the modifications which I have incorporated in this new apparatus, besides the better support of the gas receptacles and stop-cocks, is a manometric scale. In the older apparatus it consisted of a narrow strip of paper, with no light background, which made the reading of the oscillation exceedingly difficult. The scale in the new apparatus is made of a broad strip of milk glass, which at the same time serves as a background to make the reading indicated by the colored liquid more easy.

The manometric scale is divided into 50 cm., 25 cm. above and 24 cm. below zero, indicating respectively negative and positive pressure. To make the reading as easy as possible, every division has a number, and the 5, 10, 15, 20, and 25 are cut in larger and heavier figures. The old apparatus does not indicate all numbers, only 5, 10, 15, etc.

To increase the pressure, the rubber bulb in this apparatus is smaller than in the one heretofore on the market; this is for the purpose of better control when it is desired to use a little more pressure in the flow of nitrogen. The reason for having two intervening glass tubes in the rubber hose connecting the pleural cavity with the apparatus is to enable the operator to see at once if the needle is drawing fluid serum, pus, or blood. It was a peculiar accident which made me see the necessity of this modification in the connecting hose. Prior to practising the pneumothorax operation myself, I decided to see as many experts operate as possible. For this purpose I had visited a colleague in a neighboring State, who operated on a case in my presence. When the needle was inserted, the manometer rose and fell to a considerable degree. My colleague, who has had a large experience in artificial pneumothorax, stated that he could not account for the behavior of the manometer. He turned on the gas-cock, but no gas would flow. He finally gave up the operation and withdrew the needle, and the patient left the table neither better nor worse for the experiment. When the doctor tried to clean the apparatus and needle, he discovered the connecting tube to be full of pus. This explained the peculiar behavior of the manometer, and gave me the inspiration for the employment of the intervening glass tube.

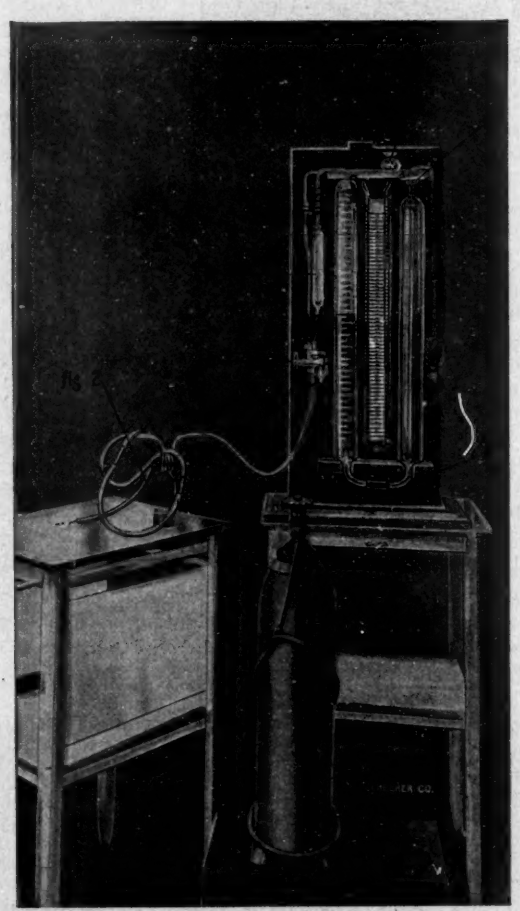
For the benefit of those not familiar with the apparatus, the following is a summary of its workings: (See illustration.)

The apparatus, in a general way, consists of two glass tubes 24½ inches high and about 2 inches in diameter. These two tubes are joined by means of a rubber hose under the base *A*.

The tube at the left is graduated to 1000 c.c.

The two receptacles are filled with water up to 500 c.c.

The graduated tube to the left hand is filled from the tank with the gas to be introduced into the pleural cavity by the weight of the water in the tube, or by additional pressure, the latter being obtained from a double rubber bulb. The flow of gas into the



intra-pleural space is slow but steady. The graduated tube is connected with a glass tube containing sterilized gauze *B*, serving as a filter. It has a ground-glass stopper, which can be removed for the renewal of gauze or cotton.

The filter communicates with a two-way diagonal-passage

glass stopcock *C*. Stop-cock *C*, when turned with the arrow downward, connects the instrument to the gas supply tank (nitrogen or oxygen) by means of a rubber tube. The stop-cock, in the same position, serves for the introduction of the gas into the intrapleural cavity.

When stop-cock *C* is reversed, that is, with the arrow pointing upward, it is connected to the manometer by a thinner glass tube, mounted between the large glass tubes, thus showing the oscillation when the needle is in the intrapleural cavity.

When the arrow of the by-pass stop-cock *D* is pointing horizontally it permits the manometric reading, showing the degree of oscillation while the gas is still flowing provided, of course, that the arrow of stop-cock *C* is turned downward.

When filling the instrument with gas, the rubber hose from the tank should be connected to the outlet below stop-cock *C*. Stop-cock *D* should stand vertically; the arrow on stop-cock *C* should point downward; stop-cock *E*, on the top of the non-graduated tube, should be turned horizontally to the left. When the flow of gas is no longer desired, stop-cock *C* should be turned so that the arrow points upward. If additional pressure is desired, stop-cock *E* must be turned with arrow pointing upward.

Funnel *F* connected with the manometer serves for the filling of the manometer tube to zero with an alcoholic solution of methylene blue.

The illustration shows a transportable tank of nitrogen containing 25 cubic feet, which is equal to 175 gallons, or 700 liters, under the pressure of 1800 lbs., per square inch. The same size tank, containing oxygen under similar pressure, can also be procured. While nitrogen may be obtained more cheaply from the air or with the aid of pyrogallic acid, the use of the tank will be found more convenient and simple.

Owing to the high pressure under which nitrogen or oxygen is held in the tank, great care should be exercised that the liquid is not blown out of the glass tube when filling the apparatus. The surest way is to have an intervening rubber bag into which the gas flows first, and from which it can gradually be pressed into the receptacle of the apparatus; but with care the flow of gas from the tank can be regulated so as to avoid accidents. The flow should always be regulated prior to attaching the receptacle to the apparatus.

In addition to this new apparatus, the illustration shows a device which will eliminate at least one of the unpleasant features which occasionally attend primary as well as subsequent operations for artificial pneumothorax. The distress which the patient sometimes feels, manifesting itself in anxiety, intense dyspnea or cardiac pains, and which is due to the expansion of the nitrogen which has been injected at the temperature of the room. The much higher

temperature of the thoracic cavity causes the gas to expand and thus increase considerably in volume. To eliminate the possibility of this accident, a coil of metal tubing is suspended over an alcohol lamp (see illustration), through which tubing the nitrogen gas is passed before it enters the pleuritic cavity. Pneumonia has been said to have been produced by the inhalation of cold oxygen, hence it is suggested that when oxygen is chosen as the gas to be injected for the production of artificial pneumothorax, it should be passed through a heated coil of metal tubing, after the alcohol flame has been extinguished, to avoid any possibility of explosion.

Robinson and Floyd state that the warming of the nitrogen will materially aid in preventing a "pleural reflex."

As to the manner of producing artificial or therapeutic pneumothorax, all antiseptic precautions, sterilizing of hands, needles, and field of operation, should be rigorously adhered to. While the operation is seemingly slight and many times accomplished without any accident whatsoever, serious and even fatal accidents have happened. Therefore, the operation should be performed either in the home of the patient or in the hospital, but never in the physician's office.

Furthermore, one should not undertake to treat a patient by compression of the lungs unless the latter is informed that it will take a long time and probably many inflations before a successful compression is obtained. He should also be told that the operation is not always successful.

To avoid accidents from shock, infection, or even temporary discomfort, the patient should be prepared by having his bowels moved. Prior to the inflation a quarter of a grain of morphine should be injected. The skin should be rendered aseptic by tincture of iodine. A local anesthesia of the skin should be produced by ethyl chloride, prior to the insertion of the needle for the injection of novocain, to anesthize the muscular layers of the thorax.

Before beginning, the apparatus should be tested to see that it is working properly. Since it is not always possible to locate a point free from pleuritic adhesion, several punctures may be necessary before the manometer indicates free oscillation, which means that the needle is in the interpleural space. Large needles which require a preliminary incision into the skin and thoracic muscles may lead to septic infection, particularly when several incisions become necessary. A finer needle is not likely to do serious damage, even if it does enter the lung. The regions which are apt to be more frequently free from pleuritic adhesions are along the axillary lines. The Kny-Scheerer Company have manufactured for me a moderately fine needle, which by means of a cap can be easily attached to the rubber hose connecting with the manometer or gas receptacle.

The patient should be placed on his side, with the arms up,

so as to widen the intercostal space. The needle is then slowly inserted through the skin and muscular layer in such place as percussion and auscultation had showed a seeming freedom from adhesion. When the needle penetrates the parietal pleura, free from adhesion, a peculiar resistance is felt, which might be likened to the passing of a needle through stretched parchment. When the manometer indicates a negative pressure, with free oscillation the gas is allowed to flow.

As an initial inflation, perhaps not more than 500 c.c. should be injected, except when the injection is made for uncontrollable hemorrhage, then larger quantities may be indicated.

To avoid gas embolism, it is advisable to begin with an inflation of 50 to 100 c.c. of oxygen. In cases of uncontrollable hemorrhages the more oxygen injected the better the patient feels from the operation. Dr. Mary E. Lapham,[2] who has had a large experience with artificial pneumothorax, recommends the substitution of oxygen for nitrogen whenever the introduction of the latter gas causes dyspnea and cardiac distress.

As stated above, it is best to inject small quantities of gas at the beginning (about 500 c.c.) This, as a rule, suffices to give the desired relief, reduces temperature, and influences cough and expectoration favorably. Robinson and Floyd, however, give as a maximum for the first injection 1000 c.c., and Bonniger[3] as much as 2000 c.c. in a strong man and 1600 c.c. in a woman. Concerning this, King and Mills[4] say: "These larger quantities seem to us unnecessarily heroic, and not altogether devoid of embarrassing sequela if not of danger." In regard to the subsequent injections, the latter say: "Subsequent inflations had best be made at intervals of not more than a few days, until the manometer readings are neutral or slightly positive and the *x*-rays show as complete a lung compression as is possible. After this is accomplished, the intervals between the injections are governed by symptoms, especially the amount and character of the sputum, temperature, etc., and by the *x*-ray. If atmospheric air is used, the intervals will necessarily be shorter than when nitrogen is employed."

Atmospheric air should never be used unless it is passed through the filter referred to in the above description of the apparatus and rendered sterile.

Before referring to the indications and contra-indications, it may be stated that sometimes the most careful injection is followed by an immediate surgical emphysema. When the beginning of such a complication arises, the emphysematous area should be encircled by a rubber bandage, which usually suffices to control

[2] Artificial Pneumothorax, New York Med. Journ., March 22, 1913.
[3] Berl. klin. Woch., August 26, 1912.
[4] Therapeutic Artificial Pneumothorax, Amer. Jour. Med. Sci., September, 1913.

the condition. Pleuritic effusion may occur later on and should be treated in the usual way. Collapse caused by pleural reflex, intense dyspnea, or hemorrhage, should be treated with injections of morphine, caffein, nitroglycerin, and locally with spirits of ammonia, whisky, hot-water bags, and ice-bags.

The cases which justify the operation of therapeutic pneumothorax although discussed before[5] may bear repeating. (1) Artificial pneumothorax is indicated first in all such cases as have not improved under ordinary hygienic, dietetic, climatic, and symptomatic treatment. Such cases are, as a rule, moderately or far advanced.

(2) It is indicated also in those earlier cases in which there is no improvement because of mixed infection or lack of recuperating powers, or when for other often inexplicable causes the condition remains stationary or the progress toward improvement is particularly slow.

(3) In all rapidly progressing cases, whether they are treated in institutions or at home, and in whatever climate.

(4) It is indicated for all patients of the moderately or far advanced type, within or outside of institutions, who are discontented, feel that not enough has been done for them, and who are desirous to have artificial pneumothorax tried.

(5) It is indicated in uncontrollable hemorrhage or chronic sanguineous expectoration.

(6) In that group of cases, which King describes as uncomplicated unilateral phthisis, with slow or subacute course, regardless of the degree of lesion, but with such pleuritic adhesion as may be removed by artificial pneumothorax.

(7) In cases of bronchiectasis, when climatic, hygienic, and the ordinary symptomatic treatment fails, it is justifiable to try the injection of nitrogen gas, with a view of producing artificial pneumothorax. There are a few cases on record where this means has been successful.

Bilateral involvement, if one lung is more involved than the other, is not a contra-indication to the production of artificial pneumothorax. Those who see many tuberculous cases, both in private and hospital practice, will admit that tuberculosis limited to one side is rare in patients who have had the disease for any length of time. In my service at the Riverside Hospital Sanatorium, where from 300 to 400 cases are treated in the second and third stages of the disease, it is doubtful if there is one in whom the tuberculous lesion is confined to one side. Most of the cases operated on in sanatoria and hospitals have had bilateral lesions, and a fair number have shown gratifying results.

Interesting and paradoxical as it may seem, all clinicians doing artificial pneumothorax work have frequently noticed that in spite of the increased activity of the less involved portion of the

[5] Knopf and Lapham, Artificial Pneumothorax, New York, Med. Journ., March 22, 1913.

lung, as a result of compression of the other side a concomitant improvement has resulted in this non-treated part of the pulmonary lesion.

Casts and albuminuria are not necessarily a contra-indication, but, of course, one must be guided by the general condition of the patient. When the lesion of the less affected side is a basal one, some authorities consider this a contra-indication. In the opinion of Dr. Lapham, this condition is not an absolute contra-indication, and the production of artificial pneumothroax is permissible because of the relief which it gives to the patient.

There are of course decided contra-indications to the production of artificial pneumothorax:

1. An extensive involvement of both lungs.
2. When there is so much cavitation in the affected lung that there is danger of the needle entering a cavity.
3. Dry pleurisy or pleurisy with effusion.
4. Myocarditis, other serious cardiac complications, or serious renal complications.
5. Pulmonary tuberculosis complicated by any constitutional disease which in itself is sufficient to inhibit all possible chances of recovery.
6. When there is an ascites or a distention of the abdominal cavity due to gases in the stomach or intestines, artificial pneumothorax must not be produced until this condition is remedied, otherwise a serious dyspneic condition and heart complications might ensue.
7. When the patient, in no matter what stage of the disease, is too apprehensive and strongly objects to the performance of the operation, it should not be resorted to.
8. Finally I would wish to say artificial pneumothorax is contra-indicated in early and favorable cases.

There are a few clinicians who, because of their success in advanced cases, recommend its use in early unilateral lesions. My experience and knowledge up to this date make me consider an early lesion of pulmonary tuberculosis a contra-indication and not an indication for the performance of artificial pneumothorax. Such early uncomplicated cases, with relatively little envolvement, should be treated by the well-tried sanatorium methods in special institutions or at home. Artificial pneumothorax can as yet only be classified as a valuable therapeutic means in a limited number of cases of pulmonary tuberculosis, but it cannot be considered the treatment of this disease in all stages.

TONSILLAR INFECTION:

A PRELIMINARY REPORT CONCERNING THE PASSAGE OF ANTHRAX BACILLI THROUGH THE TONSILLAR TISSUES AS DETERMINED BY EXPERIMENTAL RESEARCH.

By George B. Wood, M.D.,

PHILADELPHIA.

(From the John Herr Musser Department of Research Medicine, University of Pennsylvania, and the Laboratory of the Pennsylvania State Live Stock Sanitary Board.)

The determination of the importance of the tonsils as a gateway for cryptogenic infections is one of the most difficult problems in the domain of the laryngologist. Notwithstanding certain sporadic outbursts of conservatism, both from specialists of repute and from those who by striking fire desire to gain fame, the progressive clinicians are becoming more and more convinced that the tonsillar masses of the throat are responsible for a large number of general systemic infections. It takes a long time, careful observation, and many reconsiderations to arrive at the truth of a difficult subject through clinical study alone, hence the necessity of recourse to animal experimentation. The disadvantages, however, of this method are manifold, especially so when we come to study tonsillar tissues. Practically the only available animal which has a tonsillar structure sufficiently large and easy of approach for study is the hog, but unfortunately the hog is one of the most resistant of animals to the invasion of microörganisms. There are, however, certain diseases to which this animal is subject, and it was thought that by using the specific organism of one of these diseases the importance of the tonsillar tissues as a gateway of infection might be studied experimentally.

In 1904 I published the results of a series of experiments on tuberculosis. In those experiments I confirmed certain results, previously obtained by Ravenel, showing that the tonsils of the hog are readily inoculated without trauma by simply bringing tubercle bacilli in contact with the mouths of the crypts. Ravenel found that the tonsils were always infected where tubercle bacilli were present in the food. In my own work I rubbed a swab saturated with an emulsion of tubercle bacilli over the tonsils and always obtained a successful inoculation. I might state that in no instance was any other portion of the pharyngeal mucosa involved. As far as the tuberculosis is concerned, these results have been verified by the clinical and postmortem examinations of human tuberculous subjects. It is safe to say that at least 90 per cent. of all people dying from pulmonary tuberculosis show

secondary involvement of the tonsils. Also, as shown by a collective study, the average proportion of primary tuberculosis of the tonsils in children is from 4 to 5 per cent. of all tonsils removed by operation.

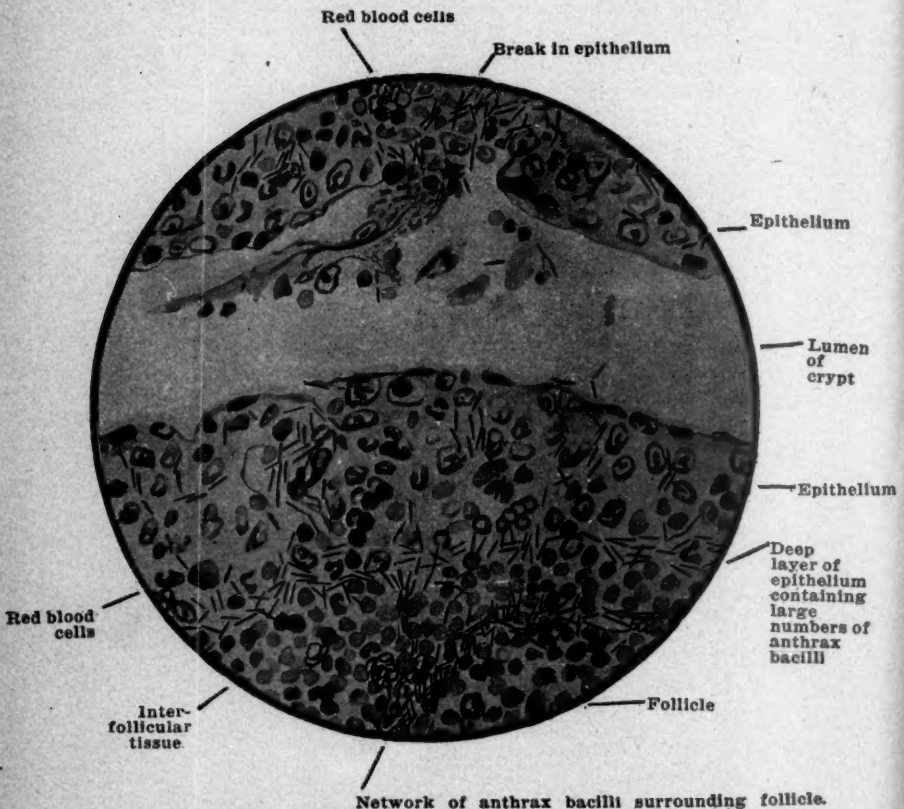
These results, however, do not warrant the assumption that the tonsils are open to a similar invasion from other organisms, and especially from those causing acute infections. In our study of tonsillar invasion we must remember that only pathogenic bacteria can be considered, and in experimentation it is frequently found that bacteria pathogenic to man are not so to animals. For instance, a strain of streptococci obtained from a case of acute rheumatic arthritis was injected directly into the blood of a hog. This was done to find out whether lesions similar to those in man could be reproduced in a hog, and if such lesions developed an effort was to be made to determine the possibility of the tonsils acting as a portal of entry. Unfortunately for the experiments, the inoculated hog flourished and grew fat under doses that would have proved fatal to almost any other animal. It was, therefore, necessary to choose an organism of known pathogenicity to the hog. The two which seemed most likely to afford results were the anthrax bacillus and the bacillus of hog erysipelas. The former was easily obtained and possessed certain advantages, namely, its ready staining in tissues and its easy culture on ordinary media, and was therefore selected for the work outlined in this paper.

Anthrax is a contagious disease commonly found among the domestic animals, frequently appearing in epidemics. It occurs sporadically among hogs, but never in the epidemic form, and it has been shown that certain breeds of hogs are more resistant to the invasion than are other species; also the adult animal is more resistant than the young, and it is probable that individuals show varying degrees of susceptibility. Among hogs pharyngeal anthrax is by far the most frequent variety. Occasionally the source of infection is through the intestine and then the symptoms correspond to inflammation of these organs. The course of the disease is very rapid, and the animals generally die in from one to two days, though sometimes they will live several days or a week. In pharyngeal anthrax the portal of entrance is always the tonsils. It has been reported that the base of the tongue and the pharynx are occasionally the atrium of infection, but there is no proof that such is ever the case.

EXPERIMENTS. The first two hogs used in these experiments had previously been inoculated into an ear vein with a strain of streptococci, taken from a case of acute articular rheumatism. This was done to determine the susceptibility of the hog to rheumatic infection. There was, however, absolutely no reaction either local or general.

Hog No. 1. Animal weighed about fifty pounds, and was in good condition.

March 14. The surface of the tonsils, especially the right, was rubbed over with a twenty-four hour culture of virulent anthrax bacilli. (The culture had not been previously emulsified.)



Penetration of anthrax bacilli through the living epithelium of a tonsillar crypt.

March 15. Animal was killed with chloroform. Cultures were made from the prescapular, submaxillary, subparotid, and retropharyngeal lymph nodes, also from cut surfaces of each tonsil. The tonsils were removed and kept for histological study. Except for a slight congestion of a small part of the right tonsil, there were no gross lesions.

All the cultures from the lymph nodes, after having been incu-

bated for two days, remained sterile. Cultures from the tonsils showed staphylococci and other organisms, but no anthrax.

Histological examination of the tonsils showed normal tonsil structure, except that a few of the crypts possessed an excess of polymorphonuclear leukocytes. In a few crypts staphylococci were found, but no anthrax bacilli could be seen anywhere.

Comment. This was a negative experiment, and a possible explanation of the failure of inoculation was that the bacilli were not first sufficiently separated before they were applied to the surface of the tonsil.

Hog No. 2. Animal weighed about fifty pounds, and was in good condition.

March 18. Tonsils were swabbed with an emulsion of anthrax bacilli, most of it being rubbed into the right tonsil.

March 20. Animal was killed with chloroform. Cultures were made on agar from both tonsils, the left subparotid lymph node, the left retropharyngeal lymph node, the left prescapular lymph node, the right retropharyngeal lymph node, the bronchial lymph nodes, the lung, the spleen, the liver, and the kidney. Bouillon cultures were made from the blood, the stomach, the large intestine, and the small intestine.

The *tonsils* were flecked with fibropurulent exudate, apparently coming from the mouths of the crypts. On the left tonsil there was a coalesced area involving about one-quarter of the tonsillar surface. The tonsils were slightly swollen and protruding on the surface. There was no distinct congestion to be seen from surface examination, but on section there were definite inflammatory striæ running through the parenchyma from the surface toward the base. A few small abscesses were found in the tonsillar substance.

The *cervical lymph nodes* were normal.

The *lung* showed scattered throughout its substance a number of circumscribed, congested, and slightly edematous atelectatic areas. These were more numerous in the right than in the left.

The *bronchial lymph nodes* were normal.

The *liver* was normal.

The *spleen* was normal.

The *kidneys* were normal.

The cultures from the right tonsil showed staphylococci and anthrax; from the left tonsil, anthrax. There was no growth on the cultures from any of the other organs, nor from the blood and the gastro-intestinal tract.

Histological Examination. Both tonsils showed somewhat similar lesions, though the infection was very irregularly distributed. While the greater part of the tonsillar structure was normal, almost all of the crypts contained an unusual amount of cellular debris, polymorphonuclear cells predominating. There were, however, some lymphoid cells and a large number of epithelial cells. In

a few crypts, staphylococci were present in large numbers and a few anthrax bacilli could be seen. The large majority, however, of the crypts contained no visible organism, even where the surrounding walls and tonsil parenchyma were extensively invaded. On the surface of the tonsil the predominating organisms were cocci, generally staphylococci, a few small bacilli, and an occasional anthrax bacillus. The surface epithelium was generally intact, though in places it was covered by a layer of necrotic tissue containing large numbers of polymorphonuclear cells and necrotic superficial epithelial cells.

Around the infected crypts the greater portion of the epithelium was either entirely destroyed, so that only a few scattered necrotic cells were visible, or it was so infiltrated with polymorphonuclear cells and lymphocytes as to make its outline scarcely distinguishable. There was, however, normal epithelium around a part of the crypt. In some places large numbers of anthrax bacilli could be seen between unaltered epithelial cells, being more numerous in the deeper layers. Near these places, that is, where there were anthrax bacilli in healthy epithelium, the neighboring interfollicular tissue showed only a few of the anthrax bacilli. The bacilli seemed to be passing in the direction of the lymph current, and in places the lymphatic spaces and some of the smaller efferent lymph vessels were choked with a dense network.

Another important finding was that anthrax bacilli tended to accumulate around the periphery of the lymph follicles, forming in places a dense ring around the edges of the follicle, with only a few scattered bacilli in its centre or in the surrounding interfollicular tissue. In the neighborhood of those crypts, of which the epithelium had been destroyed, the interfollicular tissue and also the follicles, showed the presence of numerous polymorphonuclear cells, congested capillaries, fragmentation of both the lymphocytes, and other cells, and quite a large number of free erythrocytes. Where the necrotic action was more marked all cellular contour had disappeared and the space filled with a striated non-staining debris. Anthrax bacilli were present in this necrotic tissue, seldom, however, accumulating in any great numbers. In a few places associated with the anthrax large numbers of staphylococci were found. Some of the anthrax bacilli situated in the unstaining necrotic tissue showed plasmolysis, otherwise these bacilli stained regularly and evenly.

The histological examination of the lungs showed that in the atelectatic area the alveoli contained a considerable number of free red-blood cells. Otherwise the lung tissue was normal.

Comment. The most interesting finding in this experiment was that the anthrax bacilli passed through normal epithelium, showing a tendency to multiply in its deeper layers. In the neighborhood of this invasion there were comparatively few

bacilli in the interfollicular tissue, while around the neighboring lymph follicle and in some of the mouths of the lymphatics large dense masses of anthrax bacilli were seen. Also the disease was entirely localized in the tonsils, there being no lesion in any other organ, nor could cultures reveal the presence of anthrax bacilli. Their absence from the gastro-intestinal tract must mean that in pharyngeal inoculation if the anthrax bacilli do not soon find a point of invasion they are swept away and destroyed by some agency in the gastro-intestinal tract.

Hog No. 3. March 26. Animal weighed about fifty pounds, and had been previously infected with sporothrix, and was also suffering from a traumatic myelitis. A twenty-four hour culture of virulent anthrax was rubbed over the tonsils.

March 29. Animal was killed with chloroform. Postmortem examination showed no signs of anthrax either in the tonsils or in other portions of the body.

Comment. This hog was an adult animal, and it may be that it had developed immunity to anthrax infection some time during its life.

Hog No. 4. April 16. A twenty-four hour culture of anthrax bacilli was rubbed into the left tonsil.

April 19. Animal was killed with chloroform.

Postmortem. Tonsils. On the left tonsil there were three or four elevated areas with a central necrotic core surrounding which was a zone of hyperemia; right tonsil, only one small area as described above. The mouth, pharynx, larynx, trachea, and esophagus showed perfectly normal mucosa. There was no enlargement of the lymph nodes of the neck, and the lungs, liver, and spleen were normal. A bouillon culture was made from the heart blood and agar cultures from the left submaxillary, left subparotid, and the right subparotid lymph nodes, also from the lungs, spleen, and liver.

April 21. All the cultures remained sterile.

Histological examination of the tonsils. Except for the rather small circumscribed carbuncles the tonsillar tissue was normal. The carbuncles penetrated deeply into the parenchyma and consisted of a necrotic core surrounded by a thick zone of inflammatory reaction. The area of disease corresponded in size and extent to a large crypt, of course, involving the neighboring parenchyma. Portions of the crypt wall were still found intact with normal epithelium, especially at its deep extremity. The surface epithelium covering the diseased area was necrotic, and the superficial layers were interspersed with numerous staphylococci. The anthrax bacilli was distributed throughout the diseased area, but were more numerous in the living tissue outside of the necrotic core. They were not found in the normal tonsil structure. There was a secondary invasion with staphylococci, and in one place there was a beginning abscess near the capsule of the tonsil due to this

staphylococci invasion. The staphylococci could also be found penetrating into the lymph radicals and accumulating on the periphery of one or two lymph follicles. The staphylococci had gained entrance to the parenchyma of the tonsil through an epithelial gap in the walls of the crypts. Just how these gaps in the epithelium had been formed could not be determined, but a few staphylococci were found free in these gaps, and quite a number engulfed in polymorphonuclear phagocytes in the parenchyma of the tonsil near this opening. The most resistant tissue to the action of the anthrax toxins were the germinating follicles, and these structures could be seen almost normal where the surrounding parenchyma had been entirely destroyed. The bloodvessels also showed great resistance, and were more numerous and larger than in the normal tonsil structure. The anthrax bacilli accumulated in large numbers around some of them and occasionally were found actually penetrating their walls, entering the blood current.

Comment. It is probable that the original invasion in this case was due to anthrax, and that there was also a secondary invasion of staphylococci. The staphylococci were enabled to gain access to the parenchyma of the tonsil because of the action of the anthrax toxine. The disease had advanced beyond a stage in which the anthrax bacilli could be seen in the living cryptal epithelium, consequently the mode of invasion could not be determined by this experiment alone.

Hog No. 5. April 24, 1913. Adult animal, weighed about seventy pounds. Rubbed an attenuated (at 42.5° C. for twelve days) twenty-four-hour culture of anthrax (vaccine strain B) over left tonsil.

April 28, 1913. Animal was killed with chloroform. Heart puncture made and blood taken into a bouillon tube for culture. On the right one there was a small carbuncle and a small congested area, while the left tonsil was apparently normal. There was no lesion in any other part of the pharyngeal mucosa or in the esophagus, larynx, or trachea. Cultures were made from the right submaxillary and retropharyngeal lymph nodes.

April 30, 1913. All cultures were sterile.

Histological Examination of the Tonsils. The tonsil in the region of the carbuncle showed very interesting changes. The carbuncle consisted of a central necrotic core surrounded by a distinct inflammatory zone. In the necrotic tissue large numbers of staphylococci were found and in some places they were seen penetrating into the living tissue of the inflammatory zone. Only a few anthrax bacilli could be found in the central part of the necrotic area, though they were fairly numerous around its edges. On the other hand, in the zone of inflammation, large numbers of anthrax bacilli were found. At places they accumulated, forming dense net-works, and also showed a tendency to gather around the periphery of the germinating follicles.

The diseased area was more or less associated in its topography with the position of a crypt, although it had, of course, advanced beyond the cryptal lumen and involved the surrounding tonsillar parenchyma. In some places the relation of the secondary infection of the staphylococci to the invading anthrax bacilli could be traced. The anthrax bacilli formed a distinct line of invasion in the living tissue and behind them the staphylococci were found in the non-staining material. The advanced necrosis in this position was evidently due to the secondary staphylococcic infection.

In another crypt, some distance from the carbuncle, a pure infection of anthrax bacilli was found. Surrounding this crypt the epithelium retained almost its normal structure, and yet large numbers of anthrax bacilli were seen between the cells penetrating into the surrounding interfollicular tissue. The bacilli, while fairly frequent between the superficial cells, accumulated in enormous numbers in the deeper layers of the epithelium and in the subepithelial tissue. The crypt lumen contained quite a large number of free anthrax bacilli. Portions of the surrounding interfollicular tissue showed congestion with beginning necrosis and there was considerable edema and extravasation of red-blood cells into the diseased area. The cells in this area stained poorly and there was fragmentation of their nuclei and other evidence of karyorrhexia. The anthrax bacilli congregated around some of the neighboring lymph follicles. While in some places they formed a net-work around the capillaries, the bacilli themselves were not seen in the blood current. The surface epithelium, except directly over the carbuncle, was intact and unaltered. In a few places along its surface a number of anthrax bacilli were caught and held in particles of mucous. The surface epithelium over the necrotic area had been destroyed and here large numbers of staphylococci were found, but no anthrax bacilli were seen in the epithelium itself.

Comment.—It is evident from an examination of this specimen that the anthrax bacilli gained access to the parenchyma of the tonsil directly through the unaltered epithelium of the crypts. Having penetrated the superficial layers of the epithelium, they seemed to proliferate in the deeper layers before passing on into the interfollicular tissue. The toxins, elaborated by the anthrax bacilli, however, evidently influenced the vitality of the epithelium so that it was readily attacked by a secondary infection, and it is probable that the greater amount of destruction was due to the secondary invasion of the staphylococci. There was no evidence that the anthrax bacilli passed through the uninjured surface epithelium. The slowness in the progress of the disease in this case was due to low pathogenicity of the infecting organism, an attenuated strain of anthrax bacilli having been used.

SUMMARY. From a study of the experiments as outlined above, we find several important facts which warrant us at this time in drawing certain conclusions:

1. The tonsils in the hog are more readily infected by the anthrax bacillus than any other portion of the buccal or pharyngeal mucosa. The clinical history of this disease in the hog shows that in a great majority of idiopathic cases, the pharynx is the site of the invasion, and in all of these cases of pharyngeal disease the tonsils are the portal of entrance. In none of my experiments was there any involvement of the pharyngeal or buccal mucosa other than the tonsils. While the culture of anthrax was generally brought into more intimate contact with one of the tonsils it was impossible to limit the bacilli to the tonsillar surface and they must have come in contact with a large part of the pharynx. At the inoculation an effort was made to rub the emulsion into one tonsil only, but in only one case (Hog No. 5) were the lesions limited to only one tonsil, and in this case the tonsil affected was not the one on which the culture had been rubbed.

2. Anthrax bacillus penetrates through the cryptal and not the surface epithelium.

3. Anthrax bacillus probably always gains access to the parenchyma of the tonsil by passing through the living, unaltered cryptal, epithelium, and having gained access through the superficial layers of this epithelium it tends to multiply in the deeper layers and then pass into the interfollicular tissue.

4. Anthrax bacillus penetrating through the living normal epithelium causes a devitalization of the tissue which paves the way for a secondary infection from the staphylococci or other pathogenic organisms.

5. The rapidity of the invasion is influenced both by the virulence of the organism used and by the susceptibility of the individual animal.

Following the invasion the subsequent course of the disease is similar to that found in other tissues. The toxin elaborated by the bacili causes at first an accumulation of polymorphonuclear cells, later necrosis of the tissue cells with disintegration of the nuclei. The germinating follicles show more resistance to the disease than the interfollicular tissue. Associated with necrotic process is an increase in the number and engorgement of the capillaries, and sometimes there is marked extravasation of the red blood cells. The anthrax bacilli accumulate in the lymph spaces also around the bloodvessel walls. In some of the sections examined the bacilli were found penetrating the bloodvessel walls and a few were seen in the blood current. That these bacilli were not found in the heart blood was due to the fact that in anthrax the bacilli are held up in the capillaries until they have accumulated in numbers sufficient to overcome the vital resistance, when they are suddenly swept into the general blood stream.

ON SOME OF THE BROADER ISSUES OF THE PSYCHOANALYTIC MOVEMENT.[1]

By James J. Putnam, M.D.,

PROFESSOR EMERITUS IN HARVARD MEDICAL SCHOOL, BOSTON, MASSACHUSETTS.

In bringing forward for discussion some of the more important practical considerations and scientific principles underlying the psychoanalytic movement, I have been moved by the belief that this movement marks one of the most important advances of modern medicine. It may need modification, supplementation and safeguarding, and its limitations will surely need recognition, but it cannot be ignored and it must be fostered, not by neurologists alone, but by physicians of all sorts, to whom patients with psychoneurotic symptoms constantly apply for relief, and whose advice is sought with reference to the education of children who might readily become patients at a future day. It should be seen to be wrong, now that the causal mechanism of these disabling illnesses is so much better understood, that physicians should go on laying the chief emphasis, in explanation and treatment, on incidental disorders of some special organ, or on some abnormality of nutrition, or on the need of rest, or of suggestion or persuasion, provided the chance is at hand of getting nearer to causal influences which are far more fundamental. Various circumstances may compel the ignoring of these conditions, it is true, in given cases, but this should be done with the eyes open, and will become less often necessary when more men of high standing have been encouraged to fit themselves as experts for this work.

The psychoanalytic method of treatment is not simply one more means of palliation. It is based on a recognition of the fact that these patients are suffering from emotional conflicts the nature of which they cannot understand unaided, and is an attempt to make it possible for them to extricate themselves, through self-study and self-education, from the effects of these conflicts. It is not, furthermore, in its essence, a method which is dependent for its success on some unmeasured and subtle personal magnetism emanating from the physician. On the contrary, it is a system which anyone can learn who is willing to take the pains needed for this task. As a part of this system, the personal reactions of patient and physician on each other are made the subject of careful scrutiny, and subjected to constant control. The constant aim of every well-trained psychoanalyst is to encourage the patient to assume the responsibility for the success of the investigation, and to see that it shall result in a sense of complete independence on his part.

[1] Modified from a paper of the same title presented at the meeting of the Association of American Physicians, May, 1913.

Care should be taken to distinguish sharply between the merits of the psychoanalytic method as such, and the mode of its application in particular cases. Many physicians approve of the former, who think there is reason to criticize the latter, and such physicians owe it to their patients to test the correctness of this attitude by conscientiously studying the method, making it the basis of their practice, and applying to it such tests as they desire. No one can question the importance of a thorough anamnesis[2] as the foundation of a thorough treatment, and every student of human nature is aware that a man who is struggling with internal problems and false reasoning is in no shape to meet and solve external problems. But the aim and object of this method is just the securing of an anamnesis, of a thoroughness such as has never before been attained or even tried for, and the bringing home to each patient, in a form which admits of no misunderstanding (not only of reason but of feeling) the real nature of the conflicts through which he passed in childhood and is still passing. These internal conflicts form the natural problems in terms of which every growing child ought to build his rational and moral character, and a pyschoanalytic treatment is simply one phase of a concentrated rational and moral education.

The results of the conflicts of our childhood do not die and disappear. On the contrary, they live forever, in an active form, and continue to produce effects, as integral forces, interwoven with the living fabric of our temperaments and characters, as determinants of our thoughts and conduct. It is, therefore, difficult to see why any student of education should fail to welcome this new means of rendering these conflicts clear and bringing them face to face with the intelligence and the moral sense.

It is often asked, "Of what benefit is it to make the patient intellectually aware of his long since repressed and forgotten emotions and temptations, and the frailties of his youth?" "Simply to see the terms and bearings of even a present temptation or perplexity is not equivalent to overcoming the one or solving the other; and as for bygone temptations and perplexities, once inadequately met, to be forced to rediscover them is to be made painfully aware of weaknesses which would better be forgotten and ignored. Repression is useful as well as harmful; it is a means of progress which was instinctively arrived at and found practically useful." Such is the general character of the argument.

But, in fact, although the intellectual presentation to one's self of the bearings and nature of a present perplexity or temptation is not equivalent to a moral or a rational victory, yet to arrive at such a presentation is the first step toward the victory, if the

[2] I use the word anamnesis only in the most general possible sense, and am well aware that it does not appropriately describe the outcome of a psychoanalytic investigation.

person tempted or in doubt really intends to make it such. And what is true in this respect of present conflicts is true also of old conflicts. For the latter still exist, and form, in reality, the main basis of the former; and arguments to the contrary, of the kind just cited, are apt to be only one of the many instinctive resistances that are built up as defences to preserve a *status quo* of invalidism, which is maintained by virtually the same influences that originally gave rise to it, and that made of it a means of compromise. Furthermore, it should be remembered that the final purpose of a psychoanalytic treatment is to conduct the patient's memory and insight back to that distant period of childhood when it was a question, not of being false to an obvious moral obligation but rather of slipping, half unwittingly, under the dominion of a strong craving, which then continued to make its power felt, by virtue of assuming ever new disguises. The patient—every person—must assume, later, it is true, the moral responsibility for the deeds and thoughts of this period of childhood, but if he is fortunate he may do so under the guidance of knowledge and of reason, and in doing this he may often work off his cravings, by stripping off their disguises, one by one, until it becomes clear just what it is that is leading him astray.

As for the assumed usefulness of "repression," it should be remembered that this is a word, like many more, of double meaning. It is a good thing to repress, on rational or moral grounds, and in the interests of sublimation, the desire to yield to a temptation which one clearly sees; it is a poor thing to close one's eyes to a temptation to which one really yields. One cannot, at one and the same time, cultivate real progress and likewise indulge in immature modes of thought and conduct which are hostile to progress in the best sense. The attempt to do this, even though unconsciously made, results in one or another form of compromise, which takes the shape of nervous symptoms or defects of character, both of which are often clearly traceable to the mechanism outlined.

It is well known that there has been a strong feeling of hostility to this movement on the part of some physicians, side by side with a strong confidence in its promise on the part of others, and that among its best adherents eminent pyschologists and laymen of broad culture are to be found. An association largely made up of men whose work lies sufficiently outside of neurology and psychiatry to enable them to look at the matter with unprejudiced eyes should form a fair court of appeal, so far as this is possible where expert training is lacking. It would be impossible to discuss here all the grounds of the hostility to which I have referred. I shall have something to say later on the one point which really lies at the root of all the opposition, namely, the sex question; but I pause here to consider briefly one argument of another sort. It is not infrequently urged that patients are made worse by this

treatment, and individual cases are cited in verification of this statement. It is true that the very influences—partly innate, partly incidental, and largely of the sort here indicated—which induce the serious illnesses here in question, tend to weaken these patients' powers of coöperation and will to coöperate, so that the physician's mind must be made up for many relative disappointments; and it is easy to see how the hostile opinions to which I have alluded have arisen. If, however, adequate care is taken in the choice of patients, if the physician is well trained, and if the patient is in earnest, some good is almost certain to attend their combined efforts, even when complete recovery is impossible. Good results are not obtainable with equal ease in the case of all varieties of the illnesses for which this treatment has been used. It is generally conceded that the phobias and anxiety-neuroses are the most curable forms, while the compulsion-neuroses are less amenable, and the well-marked hypochondriacal cases still less so.[3] But even the compulsion-neuroses yield more readily to this mode of treatment than to any other. That some patients do cling instinctively to their illnesses, and are ready enough to assume a hostile attitude toward the physician, or to minimize his part in bringing about improvements, is well known to everyone who has to deal, through any method, with pyschoneurotic patients. An illness, unpleasant though it be, is sometimes instinctively felt to secure a better equilibrium and greater freedom from discomfort and from the necessity of struggle, than any substitute which appears to be in sight. This reasoning is, of course, unconscious on the patient's part, but it may affect his attitude, none the less, and he must learn to recognize this fact if he wishes to get well.

These statements may serve as an introduction to the next proposition, which has reference to the difficulties which the physician must encounter in fitting himself for adequately carrying out the psychoanalytic treatment. Except for these—very real—difficulties, the records of more frequent and thorough tests of the method and a greater number of critical comments based on personal experience, would doubtless have appeared.

While the first point that needs ever renewed emphasis is that through this treatment, as through no other to anything like the same extent, patients suffering from obsessions, morbid fears, and kindred symptoms can usually be enabled to see, and often to overcome their troubles, the next point is, then, that this task, though full of interest for both patient and physician, is not a light one. Any intelligent, careful person may utilize to some extent the principles worked out by the leaders of this movement, and may, through prudence and caution, avoid exciting in the patient, in

[3] See a review of extensive experience by Dr. William Stekel, Zentralblatt f. Psychoanalyse und Psychotherapie, 111 Jahrgang, Heft 6–7, 1913.

any serious degree, the sense of dependence on the physician ("Uebertragung") which has so often proved a formidable objection to every kind of mental therapy; yet it is a very different affair to carry through really difficult cases to a successful issue.

Fortunately, the student of the future will have the great help of a comprehensive literature, and of the papers of practical advice which Freud and others have published during the past few years, and will, it is to be hoped, continue to publish. A careful reading of these admirable commentaries would make it clear to anyone that it is not alone a theoretical knowledge on the physician's part of the psychology of the "unconscious," and not alone technical skill, that is necessary for success, but that there is need also of self-restraint, patience, sincerity, and inflexible confidence in the ability of the patient to reveal himself, to his own advantage, if his will to do so goes deep enough, and the thorough-going adoption of the principle that no considerations of temporary satisfaction, on the part of patient or physician, should be allowed to override the main issues of the treatment, but that, on the contrary, both patient and phsyician should recognize from the outset that the task before them may call for material sacrifices on both sides.

It has, indeed, come to be recognized more and more by the leaders of this remarkable movement that one prominent cause of disappointment is the existence of defects or peculiarities of character and temperament on the physician's part, which blur the mental image that he seeks to form of the real patient, and unfit him for developing the patient's own powers as he might otherwise have been able to do. Few persons are so well endowed by nature as to be free from the liability to get these distorted images, and it is now looked upon as very important, indeed almost essential, that the pyschoanalyst should himself have been through the same sort of self-examination, under the supervision of some expert, that he proposes to make use of for his patients. With such thoroughness in preparation presupposed, this field of work is certain to become more and more attractive to men of the best stamp.

The psychoanalytic movement, at its best, so far from tending to encourage lower ethical standards on the part of the physician, the patient, or the community, is certain to exert the opposite tendency. For every conflict implies an antagonistic action of two interests, one of which is certain to be more in the line of the best progress than the other. It is true that the progress which a patient makes in getting well is not necessarily of a very high sort, since the forces represented in some of our human conflicts may be between tendencies both of which might be characterized as relatively selfish. But, on the other hand, issues necessarily present themselves in the course of every psychoanalytic treatment,

which have to be met through the exercise of qualities of a better kind than those that had previously been most prominently in play, and frequently the moral influence of the treatment goes very much beyond this minimum. Psychoanalysis was primarily introduced, it is true, solely as a means of ascertaining the contents and influence of those tendencies in our lives of which it can be said, not only that they lie outside of consciousness, but that they are under the ban of "repression," and yet remain as objects of unconscious desire or craving. To render a person clearly aware of such tendencies as these is the first step toward making it possible for him to modify them and to utilize his knowledge for the evolution of his character. The task of the psychoanalyst has usually been considered to cease with the accomplishment of this first step. If he goes farther and helps the patient to study not alone the repressions of the sort thus far considered—that is the repressions of sensuous cravings—but also the dimly felt and crudely symbolized longings, intuitions, and aspirations, such as every person experiences but often regards with suspicion, incredulity, and even dread, and, in a sense, may be said to repress, yet which, if scrutinized and encouraged, may form the basis of fine character; if the psychoanalyst helps to the evolution of these *quasi* repressed tendencies, he becomes an educator in a far wider sense[4] and thus enters on a line of work which entails new responsibilities and new necessities of preparation. Psychoanalysis is based on no system of ethics, and is committed to no special philosophy of life, though it does inculcate in an intensive form the sincerity and honesty which lay a good foundation, in one respect, for further development on these lines. In itself it represents a phase of education which corresponds mainly to the analytic element in the first two portions of Dante's pilgrimage into the life of the soul. The reasons for not going farther, and working definitely for sublimation in the widest sense have been reasons of a practical and cogent sort. In the first place, few psychoanalysts—few physicians, indeed, of any stamp—have had the training needful for this purpose. They have felt, with some reason, that to give moral education is not the function of the physician. In the next place the distinctive task of the psychoanalyst is so difficult, and calls for an expert training and a scientific attitude of such special sorts, that no one could do his profession or his patients justice, it has been felt, without devoting himself exclusively to the problems coming before him as scientific expert. If he attempted more, even if qualified to do so, he might perhaps accomplish less.

[4] Froebel's remarkable scheme of education, thus far utilized almost exclusively for the kindergarten, contains a provision for rational retrospection and introspection which involves the principle of psychoanalysis. Consult Miss Susan E. Blow's recent and interesting Report on the Kindergarten.

I regard these views as sound, but do not think they altogether meet the point at issue.

Psychoanalysis is, after all, a phase of education, and has been characterized as such by Freud himself. Education is of different sorts, but the goal of every kind of education is in a measure determined by the nature, origin, and destiny of the human mind, and the psychoanalyst of the future is likely to profit greatly through the recognition of this fact. This great movement cannot steer its difficult course or accomplish its whole mission under the exclusive guidance either of biogenetic methods or of those principles which the students of the processes of inorganic nature have worked out for their particular needs, and have so often and so erroneously assumed to be final statements of the truth. For these principles do not by any means fully explain the working of the mind, nor account *for the origin* of the instincts or tropisms which are supposed to foreshadow mental action; and, moreover, the too exclusive study of these principles is liable to turn aside the attention from others, of still greater value, which refer mind, instincts, and chemical processes alike, to the influence of a self-renewing, self-active energy, seeking fuller and fuller opportunities for self-expression.

I cannot pursue this argument further here, but assert as my opinion that the study of the vitally important relationship between the life of the individual and the total life of the universe, and the adequate study of the laws of mental action, will afford a basis, of a much needed sort, for the understanding of the true place of the psychoanalytic phase of education on a more comprehensive educational scheme. It may well be that among the qualifications considered essential for the psychoanalyst of the future, certain sorts of training which are now thought little of will be included. Certainly the only logical stopping place of a complete psychoanalytic treatment is a complete "sublimation."

The psychoanalyst must indeed be a scientific expert, eager to see his special art advanced, and this need must be considered paramount to every other. But in every department of learning there are men whose powers best fit them for the exclusive study of some special problem, and others who do better service, even in detail, if they see each special problem on the background of a comprehensive scheme.

It will have been made evident by the trend of the foregoing statements, even if not already known, that the main emphasis of psychoanalytic investigation and treatment has gradually been shifting more and more toward the apparently forgotten years of infancy and early childhood—that mysterious and eventful period which is more significant than any other for the formation of character and temperament, and for the establishment of tendencies of mental reaction from which it is exceedingly difficult, afterward,

to depart.[5] No more important task lies before the psychiatrist, the psychologist, or the educator, than the study of these tendencies—both those which help toward the realization of the best possibilities of development, and those which act to turn aside or turn backward the forces through which these results might have been attained.

It is needless to say that the facts and inferences thus brought together are not wholly new; they are all the more significant for not being so. Neither can the results of psychoanalytic studies, which are of necessity made largely on persons who were preëminently handicapped at the outset, in the race toward the higher goals of life, be substituted at every point for observations made on those who have, from the beginning, been inspired by a clearer vision of these goals; nor can the experiences of the child be said to foreshadow in every respect the experiences of the adult. The adult can form and follow ideals and motives which he could not have appreciated as a child, but he must reckon, consciously and voluntarily or instinctively, with his childhood tendencies in so doing, at the cost of carrying a constant handicap if he neglects this obligation.

We are so used to seeing the greater number of our children develop rapidly on fairly satisfactory lines, so habituated to seek in them for signs of mental characteristics familiar to us and into possession of which they are to come, later, and so little used to referring the evidences of their later troubles to tendencies first emphasized in infancy and early childhood, or to form any adequate conception of what passes in their unconscious minds, that only the close observer learns to recognize the extent and number of the chances of going wrong, to which all children are exposed, and in meeting which they react in such a fashion as to establish models for the reactions of their later years.

It would seem that the infant's mind is a more complex instrument than has usually been supposed. There is reason to believe[6] that the newborn child brings into the world a certain familiarity with various feelings and sensations with which there must go a dim consciousness of himself as experiencing them. Not only this, but there is a possibility, which we probably underrate, that not only isolated perceptions, but complex, though vague, emotional states, capable of being dimly recorded in memory, may be present before and during birth.[7] Be this as it may,

[5] The most important data for a psychology of childhood based on psychoanalytic research are furnished by Dr. von Hug-Hellmuth's recent monograph, Aus dem Seelenleben des Kindes. See also review by the same author, under the title Kinderseele, in the Imago for February, 1913, vol. ii, 1.

[6] See F. Peterson, The Beginning of Life in the New Born, New York; also, Ferenczi, Internat. Zeitsch. f. Aerztliche Psychoanalyse, vol. i, p. 2.

[7] Dreams and reminiscences hinting at vague but impressive birth-memories have now been reported in considerable number.

it is certain that the infant begins quickly to classify the masses of new sensations that are poured in upon him, in accordance with principles of emphasis which are quite different from those that are characteristic of the adult, or even of the older child, who has learned to shrink with a disgust that often overshoots its proper mark, from many of the sources of personal gratification congenial to the period from which he has escaped. To the infant, it would seem that every experience, partly in virtue of its novelty, is capable of yielding a special charm; and if fear soon enters to complicate the situation, even this has a certain fascination of its own to offer. From the standpoint of the emotions based on the cutaneous and muscular sensibility, it is certain that the act of nursing, the rubbings, caressings, dandlings, bathings, the warm contacts applied to large surfaces of the body, the processes of digestion, the acts of defecation and urination (that is, especially the orifice stimulations), the chance excitation of the genital organs, the movements of the limbs, often give rise—over and above the sensations and other reactions which are usually accredited to these sources, as accompaniments of normal development—to pleasurable feelings such as every adult knows and has perhaps learned to deprecate, and to classify as "sensuous," though he may have long since dissociated them from these special causes and is unaware of the purpose which they once served. To the child these sensuous feelings are, at first, natural, acceptable, and free from connotations of deprecation. To the adult, the very thought of what might be called the nursing and diaper period of infancy is displeasing, at least in many of its details, which savor of dirt, humiliation, and dependence; and he fails to do justice to the physiological and psychological value of all these attributes of this portion of his childhood as preparing him for the important functions of his later years.

In fact, however, it is not harmful or reprehensible, but necessary and desirable, that the infant and the child should devote much attention to their own personalities and powers—that is, that they should be duly egoistic—and necessary and desirable, also, that they should find their attention engrossed, up to a certain point, by that special element in the various experiences just referred to [and their number could be indefinitely extended] to which, later, the name of sensuousness is given, with its adult connotations of reprehension. The objection is not to these emotional states as such, but only to their being allowed to play too large and too engrossing a part, that is, to their being too long cultivated, in and for themselves alone, that is, simply as a means for the intensifying of personal excitement and self-indulgence, instead of as a stepping-stone to something better. The intense egoism of childhood, which is led up to by the discovery, on the part of the infant, of his power of obtaining these sensuous forms of gratification, is of great value as a means to a normal self-asser-

tiveness and individualism.[8] But egoism has its strongly sensuous aspects, and may lead to a too literal self-love (narcissism), properly classifiable as a species of sex-craving, or, like all forms of sensuous pleasure, may induce an excessive revolt (over-sensitiveness, morbid self-consciousness or self-reprehension, etc.), which is equally objectionable and on exactly similar grounds. The child who takes the middle course of safety, and who at the same time, preserves and assimilates something of good from the contemplation of the dangers by which he is surrounded, is a child of superior order, though, fortunately, the outcome which we designate as normal admits of many and considerable variations, within a wide margin. The dangers and the liability to go wrong would doubtless be more apparent, were it not that the tendencies toward the better forms of evolution have developed an instinctive power of surmounting these dangers with relative success.

In other words, the child must be sensuous (in the best sense) up to a certain point, but not beyond. Furthermore, he must not revolt too strongly against an assumed excess of sensuousness in any particular respect; for this revolt will then become a source of danger—practically a craving—in its turn. Through his first dealings with this difficult problem of sense-pleasure, to which every month and every year adds some new element of complexity, the child forms or emphasizes a series of tendencies which are likely to characterize his acts and thoughts throughout his life. He cannot be expected to exert effectively a power of control and a sense of obligation which as yet are hardly born, and the result is that, to a greater or less extent, he is bound to develop on a double plan and to prepare himself to lead a more or less double life—the life of conscious and obvious acquiescence and social relationship and the life of private and concealed fancy and emotion. This latter life he must, moreover, lead, for the most part, alone, for there is no one who can thoroughly understand the symbolic language in which he is defining to himself his new world.

Even under the best conditions the particular kinds of pleasur-

[8] Closer students of this subject are aware that there is a group of psycho-analysts, whose main representative is Dr. Alfred Adler, of Vienna, who think that the main, fundamental craving against which the young child is compelled instinctively to strive is this very need of self-assertion, the need of feeling that he is taking his place as an individual "against all comers," and that he must at least fortify himself with a feeling that he is doing so, even at the cost of self-deceit (Sickerungstendenz). Dr. Adler takes the view that the sensuousness, or sexuality, of the child is, for the most part, only the form in which this self-assertion strives to find expression. The facts and arguments adduced by him and others are exceedingly interesting, but cannot be done justice to in this place. In general terms my own opinion is that the excessive self-assertion and the sensuousness, self-indulgences, and egoisms are, all, imperfect attempts at self-expression which has a deeper root, and in view of the fact that even self-assertion, feelings of personal relationship, are present either toward oneself, or toward others who stand in intimate connection with oneself, the sex element cannot be excluded, and will continue to represent at bottom the principal repressed element in human life, in a relative sense, at least. To say this is not to deny, of course, that self-assertion, with the "Sicherungstendenz," may be the goal for which most persons mainly strive.

able sensation that first engrossed him are likely to establish goals toward which, in unguarded moments (as in dreams and fantasies) and in times of stress, he will be likely to revert, just as we all gladly revert, in minor degrees and ways, to simpler conditions of living, for compensation or refreshment. The strength of the tendency to this reversion is measured by two factors, the intensity of the original engrossment and the degree to which it was instinctively put out of sight ("repressed"), in the first instance, so that its presence as a temptation could no longer be directly seen. For an instinctively repressed temptation is one that continues to exert its action, but in a concealed form and under new names and forms. It is this quality of engrossment, combined with this fact of its early repression, that gives the sensuous element in the life of childhood its great significance, over and above its importance as preparing for the functionally sexual life of adolescence. On these grounds the life of infancy and childhood is properly described as strongly (though, of course, only partially) "sexual:" (1) because of the sensuous elements in it which actually pave the way for a normal or an abnormal (inverted or perverted) sexual development; (2) because the child tends to take himself (self-love, narcissism) and those about him (mirror-love in a new form; premature and overstrung homosexual or heterosexual attachments) as objects of a too passionate engrossment.

Infants and children evidently differ enormously as regards their liability to be engrossed by these peculiar sense seductions, on the one hand, and in the degree to which, on the other hand, they feel, in its infantile form, the inspiration and the spirit which is to show itself later as a noble sense of disinterestedness and obligation, commensurate with the best possibilities of the future. But the existence, in a certain degree, of egoism and sensuousness (*sit venia verbo*) in the period of infancy is not to be taken as a sign of recreancy to natural trust and duty.

One great task lies before every child—to make himself a useful member of the community in the widest sense.[9] But a vastly important portion of this obligation lies in learning to play his part, suitably, in the perpetuation of the race. The incitement to this task is provided for by nature with the most jealous care, as indicated by the vast multitude of seeds that must perish in order that one may germinate. Not during adolescence alone are the incitements to the accentuation of the sex-emotions infinitely numerous and infinitely subtle; not in adult life alone is the temptation a serious one to the cultivation of pleasures, which though capable of being eminently useful, are often not only negative, but harmful, in their relation to the best possibilities of development. The incitements and the temptations to abuse of such incitements present during

[9] Loc. cit.

EMORY UNIVERSITY
THE A. W. CALHOUN MEDICAL LIBRARY

infancy and childhood, are equally numerous and all the more difficult of avoidance because unrecognized. The child who is "sensitive" or "precocious," or whose fancy is unregulated, is on the danger-line, and that child is fortunate whom, from the outset, a dim vision of his best possibilities, a dim sense of obligation to a cause greater than his own—represented by the sense of obligation to parents, nation, or to an assumed universal personality more vast and significant than these—so inspires and guides that he is able to make the sensuous pleasures of his infancy his servants and not his masters. That this result fails, with tragic frequency, to occur, is testified to by the frequency with which lives which seem to be surrounded by all the outward conditions for great happiness become the battle-ground of miseries, tempered only by longings for a better fate and also by the commonness of the occurrence of the serious neuroses and psychoneuroses, which represent the compromises of tempted childhood, half aware of its better possibilities. Fortunately, even a belated enlightenment and the chance to discuss one's inner conflicts with some one who has been trained to see them in the clearest light may still be helpful. For in proportions as knowledge, reason, and insight prevail, unreasoning and passionate emotion is apt to fade away. To give the best chance for the reinstatement of knowledge, reason, and insight is the function of the psychoanalytic treatment.

What is true of the sensuous element in the period of infancy is quite equally true of various more complex groups of emotions, which are closely related, in genesis, to those just mentioned, but are more characteristic, though only relatively so, of later periods of life. I have reference especially to the sense of power[10] or superiority or self-assertion, with its accompanying opposite,[11] the sense of inferiority and submissiveness—both of which may contain a truly sensuous element—or to the excitement of causing or submitting to pain. The complex fascination from these sources lasts, as a rule, the lifetime of every individual, and plays an important part in the determination of his conduct.

I am, however, not undertaking to describe at length the life of childhood. To do this would take us far into the nursery and the kindergarten and the playground, and make necessary a deep study of the extraordinary character of the life of fancy of even the youngest child.[12] My only purpose here has been to bring into relief the character of the problem with which psychoanalysis, as a therapeutic agent, seeks to deal. With this aim in view, I have

[10] Cf. the exceedingly interesting discussion by Ferenczi (Internationale Zeitschrift f. Aerztliche Psychoanalyse, vol. i, H. 2) of the sense of power developed in the mind of the newborn child by the conditions of his life and care.

[11] Loc. cit.

[12] Cf. the very important study by Bleuler (Jahrb. f. Psychoanalyse, etc., vol. iv) entitled Autistisches Denken.

desired to intimate that, on the one hand, and as if in the far distance, there stands a goal of possibility of individual development, to which, fortunately, every child is strongly drawn by bonds which he could not himself define and does not even realize the existence of; while, on the other hand, he must work his way along, like Ulysses passing the Sirens, like Christian passing through the Valley of the Shadow of Death, in the presence of only dimly appreciated dangers, which we are now beginning, for the first time, clearly to understand. The ordinary forms of failure in this enterprise lead to the ordinary forms of nervous invalidism, or to one or another familiar defect of character; and in every such case, at every period of development, signs are to be detected through appropriate tests, unless the process has terminated in recovery, which indicate that the original temptations to make too much of particular sense-pleasures in and for themselves, have given place to new forms of temptation in which the same emotional tone is present.[13] It is not necessary that these new and ever changing signs should point to gross sensualities of any sort. One and the same act on thought may serve to indicate, at the same moment, something of a man's spiritual nature and something of his sensual nature, and in every act or thought something of both of these elements may find opportunity for expression.[14] The more serious forms of failure lead to inversions, to perversions, and to criminality.[15] The extreme outcomes, of success on the one hand and failure on the other, in the development of the child, are determined, obviously, by strong influences which are not to be classified in any single category. These extreme outcomes are, moreover, so different in aspect and apparently so opposed in nature that when either set of them predominates, the ordinary observer may fail to appreciate that in every case both are really active. Any child may *play* criminal almost to his heart's content; and perhaps every

[13] I believe that it would be of more psychological value, instead of using the expression "emotional tone," to choose some term which should be equivalent to "generic or creative energy," using this term as it has been used technically to express an idea underlying a series of manifestations. The generic energy of a tree, for example, covers the whole series of forms comprising the cycle of growth of the tree. In other words, it would be profitable to bear in mind, as I have hinted in another part of this paper, that in dealing with these phenomena of immaturity, under the different forms in which they manifest themselves, we are dealing with forces and tendencies which might be compared analogically to other process groups with which observation has already made us familiar, as classifiable under one or another heading.

[14] It is important for the rational interpretation of the symbolism of dreams and conduct, that this point should be clearly understood. It is often urged that those who use the psycho-analytic method are too prone to read sexual meanings into trivial and harmless thoughts. But, however, this may be in a given case, it is certain that the ingeniousness of psychoanalysts in this respect does not equal the ingeniousness of persons of emotional temperament (patients, poets, and artist) in finding means to express the sensuous elements of their nature which they have brought over from their childhoods. Any symbol can be made use of by the lover to intensify his passion and find new outlet for it. But that does not prevent the employment of the same symbol for some other end or ends. These facts and their bearing would be recognised were it not that the very hint at the possibility of sex-meanings gives rise, unjustly, to opposition and resentment.

[15] It is, I trust, needless to say that I am now dealing with the psychogenetic factors alone, and that I realise fully the existence, likewise, of somatic factors.

child, as a necessity of biological and psychological development, shows tendencies which, if they persisted and grew stronger, would mark him as an invert or a pervert. But so powerfully does the current ordinarily set, in the one direction or the other, that we feel entirely safe, as a rule, as regards the future of the greater number of our children, and consider that those who go right and those who go wrong are separated by differences almost as great as those that distinguish from one another the different animal species. It is only when the chance is offered for getting at the real facts, and especially for clearly facing the repressed tendencies and experiences of the life of childhood, that these differences are seen to be of degree only, and that we learn to appreciate that all children grow up in a broad borderland between the evil (as we classify it later, not as it appears definitely to the child) and the good. Many an adult, every individual in some measure, is more or less under the spell of this or that tendency which harks back directly to one or another special craving or sense—fascination of childhood or infancy, which was then, though perhaps only for a brief period, felt in full intensity, but promptly repressed and relegated to the unconscious.[16] But by this "repression" these special cravings or fascinations are placed in a position of advantage for continuing to exert their influence, always in covert ways and in constantly changing ways, without ever, perhaps, coming under the full light of conscious, rational inspection, though constantly giving rise to emotional distresses and nameless fears, and an ill defined sense of something wrong. Strangely enough, these distresses and apprehensions are bound to the fascinations which preceded them by bonds which show them to be of common nature, and are instinctively clung to as representing, in terms of the patient's unconscious logic, the once legitimate though soon repressed pleasures of the age of childhood.

Just what the original fascinations of childhood are I have been able here only distantly to hint. Every observer will admit, however, that such fascinations exist; that they are very numerous; that every child's vivid fancy[17] is fertile in inventing them; that they might be classed primarily and broadly as egoistic; that they are of a kind that it is easier to acquire a taste for than for those which are to be useful for the higher spiritual development of the individual, and that for this reason they are constantly reverted to in times of even moderate stress. If it is just to classify as "sensuous" these vague, voluminous, personal, egoistic, mirror-love sorts of pleasures, which are ill-defined, but intense, and full of

[16] The tendency of persons of extreme refinement to show, in the deliria of mania or the ramblings of dementia præcox, a familiarity with subjects and language assumed to have been wholly foreign to their thoughts, has always been a matter of painful comment and surprise. In fact, such patients thus disclose a very important chapter in their development.

[17] Reproduced in the delirious but really consistent utterances of many insane patients, especially in dementia præcox. See Bleuler, loc. cit.

captivating thrills, it is just also to recognize that the quality which is most characteristic of them is most strongly present in those special sensations and emotions which are particularly and specifically related to the sexual functions, and which, as such, enjoy a special primacy as regards psychological and physiological significance. But these sensations, acts, and emotions—both those which are frankly sexual and those which contain the sensuous characteristics of the sexual feelings as a constituent element or are readily drawn into the great vortex of which the sexual feelings and emotions form the centre—are largely repressed, in deference, partly to the child's fastidiousness, partly to his conscience (both of which have a social root), and partly to the spoken or unspoken wishes of a social environment in which the interests of individual members are subordinated to the assumed interests of the social group, regarded as a whole.

The situation of the young child is a difficult one; and so, too, is that of the adult who is the child grown large and who is tempted to play the child's game with the grown-up weapons of the man. A man is filled with dread[18] lest he may injure some member of his family whom in fact he loves, and perhaps isolates himself in consequence. But psychoanalytic study shows that in reality he is reverting to his childhood and is playing the old childhood game of love, hate, desire, fear, anger, sorrow, jealousy, and remorse, —each emotion acting at once as the parent and the child of its opposite and each capable of passing into the other or suggesting its opposite or of intensifying itself through inducing a thrilling sense of contrast with an undefined opposite. In childhood, the first and strongest of these emotions is desire, especially, desire of the sort that is particularly characteristic of the sex-feelings and emotions, which, instead of being absent, in infancy and childhood, are both present and engrossing. And so it is that when the conscience and the will relax, and the longings hark back to less strenuous and more immature and infantile interests, the emotions which come to the front are necessarily those which it is proper to denominate as sexual, since it is round the—biologically and socially—enormously significant sex-instinct that these interests and emotions cluster, and from it that they gain their color, and their emotional tone. Having learned all these and many other kindred facts, we can no longer wonder at Freud's dictum, that no psychoneurotic (emotional) illness can possibly occur without a concomitant, and partly causal, ruffling of the vast waters of the sex-life.

In searching for a simile through which to illustrate to myself the strength of the bond by which the development of the child is restrained in this or that respect, through influences of varying sorts, I have been able to find none so useful as that of the massive

[18] I have, of course, specific histories in mind.

"fixation"[19] or "arrest" that brings about the formation of the various animal species as an alternative to the continuance of the line of progress toward higher types. It is needless to say that I attach little or no biological importance to the comparison.

When the case presents itself of helping to recovery a patient in whom these tendencies to arrest have become established, it is of great service to him, not alone to be shown clearly the path toward a better evolution of his personality and powers, but to be helped to put himself back again, in memory and imagination, at the point where the partial arrest occurred, in order that he may see clearly what a different choice, at that point, would have accomplished for him, and that he may even now make it, as if for the first time, and thus rid himself of a craving which had gained a strong and yet fictitious power over him. But these processes must be conceived in psychological terms. Each individual must learn to see himself and the physician must learn to see him, as a collection of interwoven forces, all still living and still active, even though many of them came into existence in the early days of childhood. And the physician who does not possess by nature, or cannot acquire, the power of thus reading the lives of his patients in the terms of these living forces, is not at all likely to find satisfaction or success in psychoanalytic practice.

No one can make the best use of his powers, either for his personal happiness and guidance or in the interests of the community, who is the victim of his own immature passions, prejudices and superstitions, and who continues through adult life to use his imagination for inventing an unreal world of which he is the centre and the hero. Such a person should be aided to destroy this great structure of a misguided fancy and self-love, by learning to see that from its foundations upward, it misrepresents his best desires. A sound moral education should not tend to stifle emotion but to see that it is directed toward the best goal. The child's danger is that he will misuse the great forces which are placed within his grasp, for his own personal gratification, and one form, not yet clearly alluded to, in which he does this, is in playing with his own heated emotions, under the guise of imaginary danger. Every child, even if at bottom cowardly, loves to play at the game of Phaeton, assuming, in ignorance and folly, to drive the wagon of the sun. He loves to dally with himself and to create mock dangers and mock fears, in ways that by no means necessarily fit him to meet the real dangers of the coming world. He loves to excite himself with fire and the dark, and with fancies of death and life, not realizing with what deep, emotional interests he is dealing. But this emotional fire must not be too hot. When that point is reached the fear becomes a real sense of terror, and then the child, ignorant that the cause of his putting himself into the dangerous

[19] Freud's term.

situation was his (covert) love of what the adult calls sensuous pleasures, finds himself forced to explain or "rationalize"[20] his fears. The fascinating flame becomes a "cross" to him, and he begins to refer his distress to one or another common cause of dangers. One may represent this situation by drawing a flame and a cross, side by side, on a sheet of paper, with a line between them to indicate, so to speak, that though in reality mutually dependent, each is unconscious of the other. If, now, the patient would recover, and cannot do so through the interest of work, or by the attempt to get into a spiritual atmosphere above the fear, he must learn to turn his attention wholly aside from his symptoms (his "cross"), the contemplation of which he is certain to have followed too long, and to too little purpose, and must study the flame, that is, he must study the history of his emotional life. An intimate acquaintance with this history, by teaching him the real nature and origin of his fears, and showing them to be fears of himself, puts him in a far better position for attaining that development of character through which he may get well. Then the cross, in the old sense, disappears, but may still be voluntarily accepted as symbolizing the willingness to endure sufferings, not indeed of the sort formerly endured, but of a sort which will make the patient better able to take his place as a useful member of the community. The person who has attained this development has learned, in Emerson's words, that "when half-gods go the gods arrive," the half-gods being his own immature desires. What every person wants is happiness and content. But these are to be gained, as a rule, not by the cultivation of pleasures of the kind that exist in and for themselves, but rather through disregarding them in the interests of a broader life.

It is one of the remarkable signs of the far-reaching significance of the freedom with which we are endowed that we can use it to destroy our freedom; and a striking illustration of this is seen in the subtle, instinctive keenness with which the young child, when not sufficiently impelled by his own natural resources and not sufficiently aided by education, instead of taking each stage in his development as a stepping stone to the next, grows old indeed in years, but clings nevertheless, in secret, and without fully realizing the fact, to childish forms of thought and emotion which should have been outgrown and of which, even as a child, he was perhaps secretly ashamed. Clear sighted educators have long known the importance of this principle in the case of children somewhat older than those that I have now in mind. But is has remained for this group of investigators and those who have gradually affiliated themselves with them, to dicover, point by point, the influences, which lead to the formation, in the hidden depths of the child's mind, of emotional modes of thought and feeling (Autistisches Denken, Bleuler) destined thereafter to play a large part in the

[20] Dr. Ernest Jones.

determinations of his conduct. The emotions and excitements of this autistic life exist largely, not as transitions to something better and more permanent, but in and for themselves alone. Even though not consciously perceived they act to draw the desires away from the disinterested forms of love which constitute the natural goal of progress, and tend instead to the cultivation of egoistic forms of love, which may indeed have an object, but use that object as a mirror by means of which self-love may be intensified. The fantasy-life of young children may serve as the basis of wholesome forms of religion and art, but sometimes, instead of this, it serves as the basis of morbid tendencies and morbid fears.

The evidence is very strong for the view that the appearance of the human mind among the evoluntionary forces[21] introduces a new factor of enormous import. Even the infant and young child, by reason of the endowment of their mental structure, have powers and obligations which they, however, cannot easily or fully recognize. With their consciousness of themselves they acquire also the germs of consciousness of the scheme of the universe. They acquire the sense of power, responsibility, and personality, and also of weakness and dependence upon others and the subtle pleasure that goes with dependence. With their unbridled fancy they people the world and they utilize not only sticks and stones but everything, even their own sensations, as terms in which to express their passions and desires and longings. Then come reactions, loathings, self-depreciations, and forgetting in the form of repression, which means really not forgetting but setting aside for further use. The child who is living externally a life of eminent self-satisfaction and propriety may be indulging himself, without knowing it, in the aroma of pleasures and excitements which he had banished to the "unconscious," but to which he still keeps many secret avenues open.

How can a treatment through which the patient is enabled to see what is going on and to unmask the "confidence game" played by his lower nature on his higher nature, fail to commend itself as worthy of support? The method which attempts this should, moreover, be judged with reference to its possibilities, and not to its present achievements only. Its aim, in general terms, is to help toward the solution of the external problems of human beings, by helping them, in specific ways, to solve their internal problems.

And this is a reasonable task. For the drama of the external world is played over, beforehand, in the minds and hearts of the personalities by which it is peopled. Let those who believe in the value of the method, but object to the way they think it used, test it out themselves. They owe it to their patients to attempt this task.

[21] Attention has been called by Bergson and many others ,to the significance of "life" (*pousde vitale*, etc.) as a factor in evolution. The doctrine of which I now speak includes this, but goes beyond it.

AN IMPROVEMENT OF THE BENEDICT METHOD FOR THE DETERMINATION OF SUGAR IN THE URINE.

By William Weinberger, M.D.,

ADJUNCT ATTENDING PHYSICIAN TO LEBANON HOSPITAL, NEW YORK.

(From the Biochemical Laboratory of Columbia University, at the College of Physicians and Surgeons, New York.)

Benedict's[1] sugar titration method is conducted in the following manner:

"The urine, 10 c.c. of which should be diluted with water to 100 c.c. (unless the sugar content is believed to be low), is poured into a 50 c.c. burette up to the zero mark; 25 c.c. of the reagent[2] are measured with a pipette into a porcelain evaporation dish (25 to 30 cm. in diameter), 10 to 20 grams of crystallized sodium carbonate (or one-half the weight of the anhydrous salt) are added, together with a small quantity of powdered pumice stone or talcum, and the mixture heated to boiling over a free flame until the carbonate has entirely dissolved. The diluted urine is now run in from the burette, rather rapidly, until a chalk-white precipitate forms and the blue color of the mixture begins to lessen perceptibly, after which the solution from the burette must be run in, a few drops at a time, until the disappearance of the last trace of blue color, which marks the end-point. The solution must be kept vigorously boiling throughout the entire titration. If the mixture becomes too concentrated during the process, water may be added from time to time to replace the volume lost by evaporation. The calculation of the percentage of sugar in the original sample of urine is very simple. The 25 c.c. of copper solution are reduced by exactly 50 mg. of glucose. Therefore the volume run out of the burette to effect the reduction contained 50 mg. of the sugar. When the urine is diluted 1 to 10, as in the usual titration of diabetic urines,

[1] Benedict: Jour Amer. Med. Assoc., October 7, 1911, p. 1193.

[2] The solution has the following composition:

	gm. or c.c.
Copper sulphate (pure crystallized)	18
Sodium carbonate (crystallized)	200
(Or one-half the weight of the anhydrous salt may be used)	
Sodium or potassium citrate	200
Potassium sulphocyanate	125
Five per cent. potassium ferrocyanide solution	5
Distilled water to make a total volume of	1000

With the aid of heat dissolve the carbonate, citrate, and sulphocyanate in enough water to make about 800 c.c. of the mixture, and filter, if necessary. Dissolve the copper sulphate separately in about 100 c.c. of water and pour the solution slowly into the other liquid, with constant stirring. Add the ferrocyanide solution, cool, and dilute exactly to one liter. Of the various constituents, the copper salt only need be weighed with exactness. Twenty-five cubic centimeters of the reagent are reduced by 50 mg. of glucose.

the formula for calculating the percentage of sugar is the following: $\frac{0.050}{X} \times 1000 =$ per cent. in original sample, wherein X is the number of cubic centimeters of the diluted urine required to reduce 25 c.c. of the copper solution."

In this modification of the original Fehling process, the copper, instead of being reduced to the red suboxide, which of its own color obscures the end-point of the reaction, is precipitated as cuprous sulphocyanate, a snow-white compound, "which is rather an aid than a hindrance to accurate observation of the disappearance of the last trace of blue color."

However, in applying Benedict's method to urine of low sugar content, below 0.5 or 0.4 per cent., as is frequently the case in glycosuria, one is impressed by the fact that there is no blue color at the end-point that could disappear, the contents of the porcelain dish then having a dirty, brownish-green hue, that gradually merges into brown. This renders the correct estimation of the end-point difficult, if not impossible.

This condition naturally suggested clarification of the urine, previous to titration, by the addition of lead acetate. This procedure, while helpful, requires additional manipulations and calculations. The possibility of a chemical change of the copper solution is another objection to the use of lead acetate.

None of these objections apply to the simple modification the writer has been investigating. It consists in the addition, just before heating, of approximately 10 grams (two heaping teaspoonfuls) of powdered calcium carbonate to the contents of the porcelain dish (25 c.c. of Benedict's solution, 10 to 20 grams of crystallized sodium carbonate or one-half the weight of the anhydrous salt, and a small quantity of powdered pumice stone). Thereupon the titration is conducted in the usual manner.

The snow-white calcium carbonate, insoluble and suspended in the alkaline solution, appears to act in a manner similar to that of sulphocyanate of copper, by effectively obliterating all color except the blue of the unreduced copper compound.

The end-point obtained is sharp, the blue color being visible up to the addition of the last two drops of urine that are necessary for complete reduction, a pure white residue remaining. It is necessary, however, to add a sufficient amount of calcium carbonate, about 10 grams, otherwise the residue will appear gray and the end-points less distinct.

In order to prevent sudden violent ebulition of the hot concentrated solution, it is advisable to dilute the latter with a few centimeters of distilled water.

The writer's experiments show that the addition of calcium carbonate, as recommended above, does not cause any unfavorable effect on the accuracy of the titration.

THE APPLICATION OF THE CALCULUS TO THE MEDICAL SCIENCES.

By I. J. Schwatt, Ph.D.,
PROFESSOR OF MATHEMATICS, UNIVERSITY OF PENNSYLVANIA.

In the following I am giving a few ideas on the above subject in connection with a Calculus recently published, entitled *Einführung in die Höhere Mathematik für Naturforscher und Aerzte*, by Dr. J. Saltpeter.[1] It is a book of unusual merit. The representation is rigorous and lucid. The book contains many examples illustrating the application of Calculus in developing mechanical and chemical laws and processes. Although the author has intended the book for the use of students in the natural sciences and medicine, it is equally well adapted for engineering students.

The applications of the Calculus to the different branches of the medical and allied sciences is of comparatively recent origin. The originators are still with us. The science of mathematics is new. It is only about 200 years since the Calculus was invented (Leibnitz, 1646–1716 and Newton, 1642–1727). The first account of it was published by Newton in 1693. But the real advance of the mathematical sciences has taken place during this and the last generation. The application of Calculus to any of the sciences including the technical sciences, dates back only to the middle of the last century. Most of the schools of engineering in this country and abroad have been founded within the last fifty years or so. The scientific development of all the natural sciences does not date very far back, and the makers of the sciences have died within our generation or are still living.

I recall the address delivered by the founder of scientific pathology, Rudolph Virchow, before the students of the University of Berlin on the occasion of his seventieth birthday (1891), at which he entertained his hearers with an account of the most incredible theories and absurd views that prevailed in natural science when he first began the study of the subject.

In this connection it is interesting to read the presidential address of Dr. S. Weir Mitchell to the Congress of American Physicians and Surgeons held in 1891,[2] from which I quote the following (p. 163):

"When I was yet a lad there were then alive men who could recall the day when what a patient said, and the physician saw and felt, were all that a case of disease had to tell him. The limitations they suffered under, lured or drove them into attempts

[1] Gustav Fischer, Jena, 1913.
[2] Transactions of the Congress, Vol. II, New Haven, 1892.

to classify, and minutely to multiply the signs of disease, until what they believed they saw and felt represented impossible refinements in symptomatology."

It should be distinctly understood that the operations of the so-called elementary mathematics are not sufficient for the study and the interpretation of natural phenomena and processes. This can be accomplished only by Calculus. In fact, Calculus seems to be the very language of nature. All processes in nature proceed by infinitely small degrees. Consider the growth of a tree or of any organic matter. During the interval of time required to give a glance at the tree, the tree has either grown or decayed. While this growth or decay is so small that it cannot be measured by the most delicate instruments, yet it is as definite a quantity as any finite quantity is. The growth of a tree during a month or a year is made up of the infinitely large number of the infinitely small growths during the infinitely small periods of time. Again, a vessel of water is heated. The infinitely small increase in the temperature of the water is not the same for the different infinitely small periods of time. We say the amount of growth during the different infinitely small periods of time varies. Now these infinitely small numbers which represent the infinitely small increases can be compared with each other just as finite numbers can be compared. The infinitely small increase in the temperature of the water during one infinitely small period of time might be any number of times as large as the infinitely small increase during the same or a different infinitely small period of time.

Also, just as the infinitely small quantities can be compared with each other, so can infinitely large quantities be compared. One infinitely large quantity might be a number of times larger or smaller than another infinitely large quantity. If a piece of material be divided into a number of parts and each part divided again, and if we imagine this division continued until each particle is so small that it cannot be detected by the most powerful microscope, then no matter how far the division is carried on, the particles, although infinitely small, have a definite extension and weight. The sum of the infinitely large number of the infinitely small particles make up the original piece of material. The infinitely large number representing the number of infinitely small particles at one stage of the division might be many times larger or even infinitely times as large as the infinitely large number representing the number of infinitely small particles at another stage of the division. For the term infinitely small the term infinitesmal is used.

The operations of Calculus enable us to study a process during a given period of time by means of the changes which are taking place during the infinitely small intervals of time.

Calculus is divided into two branches, the Differential and the

Integral Calculus. In the first, problems relating to infinitesimal changes are studied and in the second, problems leading to the sum of an infinite number of infinitesimals are considered. Thus: If a body is being heated at a certain rate of increase of temperature, its rate of expansion at any instant may be obtained by means of Differential Calculus. Or again, if a particle moves under the action of certain forces its velocity at any instant can be determined by Differential Calculus and the distance travelled by Integral Calculus.

Helmholtz, the inventor of the ophthalmoscope, who is as well known to the mathematician and physicist as he is to the physician, was led to the results in mathematics from the observation of nature. Professor Leo Königsberger of Heidelberg[3] says of Helmholtz: "He obtained his mathematical problems—this is certainly the only true way, but also one to be pursued by so great a master—directly from observation of nature. . . . On this account there is to be found in all his works a great many results, which are interesting even from a purely mathematical point of view, but which uncover deep and intelligible natural laws." By purely mathematical investigation based upon known natural laws, new laws have been derived which have predicted phenomena, which in turn have been verified by observation and experiment. To show what mathematics is capable of accomplishing and what might be expected of this powerful instrument if applied to the study of the human body, I cite the following instances:

One of the most remarkable discoveries in Physics—the law of conical refraction—was made as the direct result of mathematical investigation.

By means of Calculus Sir William Rowen Hamilton found that a point, when looked at through a crystalline place cut in a certain direction, ought to appear not as a point but as a ring. Lloyd, of Dublin, verified Hamilton's results experimentally.[4]

As a direct result of mathematical analysis, Professor Michael I. Pupin, of Columbia University, has invented a process which has considerably increased the distance of communication by telephone.[5]

The discovery of wireless telegraphy owes its inception to mathematics.

The old idea was that electricity could be transmitted from one place to another only by means of metallic conductors, such as wires, etc. The air was considered an insulator or non-conductor of electricity. James Clerk Maxwell, by purely mathematical deductions, arrived at the conclusion that electricity, like light, is

[3] Herman von Helmholtz's Untersuchungen über die Grundlagen der Mathematik and Mechanik, 1896, p. 2.

[4] Humphrey Lloyd, Elementary Treatise on the Wave Theory of Light, Third Edition, p. 209, London, 1873.

[5] The Electric Review, Vol. XL, No. 2, 1902, p. 53.

propagated by ether vibrations; that light, radiation and electric radiation are essentially the same and that electro-magnetic waves obey all the laws of optics. A full development of the subject is given in his work, "A Treatise on Electricity and Magnetism," first published in 1873.[6]

As Maxwell's results were opposed to the accepted views, and as his theories were only the result of mathematical deductions the most eminent men of science doubted their validity. Maxwell[7] himself said: "There appears to be in the minds of these eminent men some prejudice or *a priori* objection, against the hypothesis of a medium, in which the phenomena of radiation of light and heat and the electric actions at a distance, take place." Even Heinrich Hertz[8] (1857–1894), who ultimately became the champion of Maxwell's mathematical theories of electricity, said: "Notwithstanding the greatest admiration I hold for Maxwell's mathematical conceptions, I have not always felt quite certain of having grasped the physical significance of his statements."

In 1879, the Berlin Academy of Sciences offered a prize for a problem which practically meant the experimental verification of Maxwell's electro-magnetic theory. Hertz took up the problem and succeeded in verifying experimentally Maxwell's mathematical theories. It was, therefore, through mathematics that the so-called Hertzian waves were discovered which Marconi has made use of so ingeniously in connection with one of the most wonderful practical inventions that has ever astonished mankind.

Dr. F. H. Garrison,[9] in an admirable contribution, says: "Most of the working theorems of modern physical chemistry were stated *a priori* as mathematical consequences of the second law of Thermodynamics by Gibbs, many years before they were actually tried out, and in some cases, rediscovered in the laboratory."

Fresnel[10] (Fresnel's wave surface), in a letter to Young, said: "Without doubt I have often wanted the spur of vanity to excite me to pursue my researches in moments of disgust and discouragement. But all the complements which I have received from Arago, Laplace, etc., never gave me so much pleasure as the discovery of a theoretical truth or the confirmation of a calculation by experiment."

Mathematicians planted the first seeds of accurate and scientific medicine, but unfortunately for the science it was at a time when the sciences of physics and chemistry were only about to spring into being, when the law of gravitation was not as yet established, when Calculus was not yet invented.

[6] Clarendon Press, Oxford.
[7] Ibid., Vol. II, third edition, p. 492, 1892.
[8] Electric Waves, London, 1893, p. 20.
[9] Physiology and the Second Law of Thermodynamics, New York Medical Journal, Vol. XC p. 494.
[10] Peacock. Life of Young.

René Descartes (born in France in 1596, died in Stockholm in 1650), the inventor of the analytic geometry, was an accomplished physicist. He wrote a treatise on physiology entitled L'Homme (1662), which is said to be the first physiology published. Sir M. Foster,[11] speaking of the book, says: "But his main idea, that the problems of man ought to be treated in the same way as the problems of the rest of nature, made itself felt and produced effects in after times."

Giovanni Alphonso Borelli (born at Naples in 1608, died 1679), was one of the leading mathematicians and physicists of his day. Under him the University of Pisa became the most famous school for mathematics and medicine. The new methods of physical mathematical research led him to the study of the mechanism of the human body, which he has incorporated in a treatise on animal motion *De motu animalium*. In the preface of the book he states that his purpose in science is "to ornament it and enrich it by mathematical demonstrations."

Both Descartes and Borelli were inspired in their work by the teachings and writings of Galileo (born at Pisa in 1564, died 1642). When Professor of Mathematics at the University of Pisa, Galileo invented the thermometer or thermoscope. It is said that when Galileo was but eighteen years of age and a student in medicine, when sitting in the Cathedral of Pisa his attention was drawn to a huge swinging lamp, which still hangs there. He noticed, that whether the arc through which the lamp swung was large or small, the oscillations occupied the same interval of time. That observation led him to the invention of the pulsilogon, which, though imperfect, was hailed with wonder and delight by the physicians of the day, and was soon taken into general use."[12]

Molecular force has placed each particle of which the bones, the nerves, and the muscles are made up, in its proper place. Speaking of the molecules which make up the human body, John Tyndall[13] says: "Unless the existence of law be denied and the element of caprice be introduced, we must conclude that, given the relation of any molecule of the body to its environment, its position in the body might be determined mathematically." Mathematics might perhaps help us to discover the laws which govern the changes that take place in the cells and tissues of the human organism, and enable us to direct and redirect these changes. To understand the vital organism of the blood and to determine the blood pressure and the velocity of the blood current in the arteries and veins, a knowledge of the physical-mathematical laws of hydro-dynamics is necessary. The mechanism of labor in normal births is a physical process based on mechanical mathematical principles.

[11] Lectures on the History of Physiology, Cambridge, 1901, p. 62.
[12] Viviani. Vita di Galileo.
[13] Scientific Limit of the Imagination, London, 1870, p. 61.

Ophthalmology, the science of the structure, functions, and diseases of the eye, may be justly considered a branch of applied mathematics. A. Gullstrand of the Medical Faculty of the University of Upsala won, in 1912, the Nobel Prize for his work on the internal mechanism of accommodation to which he applies the operations of Calculus. It is of interest to note that in the Medical Department of the University of Berlin, Professor Gutzmann is giving, during this Winter-Semester, a course in *Mathematische Analyse normaler und pathalogischer Sprachklänge.*

The human skeleton, including the various articulations, is constructed in strict accordance with mathematical laws. When the end of a long bone, say the femur, is examined, it is found to be made up of interlacing osseous plates, technically called "concelli." Professor J. Engel,[14] of Prague, says: "Not without a purpose does the structure seem to differ in the various arches, the use here of vertical columns, there of oblique abutments, is certainly intended for something else than to merely delight the eye of the anatomist by pretty carvings." Professor Herman von Meyer, of Zurich, in 1867, presented before the Naturforscher Gesellschaft some specimens which were to demonstrate the inner structure of the human thigh bone. Culman, the founder of graphical statics, who happened to be present, recognized at once in the course and in the arrangement of the concelli, the trajectories of graphical statics, and he was greatly surprised at the similarity between the mysterious workings of nature and the mode of construction followed by scientific engineers. The subject of the construction of bones was next taken up by Professor Wolff, of Berlin, a man combining a thorough training as a physician with a rare knowledge and understanding of mathematics, and who was advised and aided in his work by Culman himself. He has embodied the result of his twenty years' investigation in a work, entitled, "The Law of the Transformation of Bones,"[15] which is interesting alike to the physician, the engineer, and the mathematician. He found that the shape and inner structure of a bone depended upon the direction and the amount of the stress acting upon it, and that changes in the stress will cause definite changes in the form and the structure of the bone, in accordance with strict mathematical laws. And just as a pathological stress will cause abnormal changes in a bone, so, on the other hand, a deformed bone may be made to return to its normal state by well-directed changes in the stress acting upon it. These principles Wolff has made the basis of a new method of the treatment of various deformities of bones, notably club-foot, without resorting to operative measures.

[14] Sitzungsberichte der Wiener Akademie der Wissenschaften, 1851.
[15] Julius Wolff, Das Gesets der Transformation der Knochen, Berlin, 1892.

It would appear that the present generation of physicians are not in a position to follow ideas in the medical sciences if they are represented by means of mechanical-mathematical principles. On that account, investigators of the medical sciences along mechanical-mathematical lines are often obliged to give the results of their investigations without the method by which they have arrived at their conclusion.

The discoveries of Zuppinger in the treatment of fractures of bones is based on mechanical-mathematical considerations. Dr. Th. Christen has embodied Zuppinger's discoveries in a book,[16] from the preface of which I quote the following:

"Right here an objection which we meet at every turn, that Zuppinger's ideas may be very interesting, perhaps even theoretically correct, but that they are too 'mathematical,' too 'abstract,' and not intelligible to the medical fraternity, must be answered. . . . We have, however, owing to the sentiment at present prevailing among our colleagues of the medical profession, made it our duty to keep the principal part of the text of this book free from every mathematical formula. . . . In fact a large number of therapeutical errors which are still taught and practised are based on wrong mechanical conceptions. . . . To give only an approximate idea of the importance of every improvement in this field of science it may be stated that (according to Hoffa) about two-thirds of the premiums paid in workmen's compensation insurance in Germany are the result of poorly healed fractures of bones."

In the preface to his masterly work,[17] written "in erster Linie für Mediziner und Zoologen," Otto Fischer states that he has endeavored to derive and represent the kinematic principles in an elementary way, so that the book may be more generally understood, but in Chapters IV and VI he was obliged to take recourse to the Differential and Integral Calculus, because without it he could not obtain the principles sufficiently general and intact.

Dr. Friedrich von Müller, Professor of Medicine in the University of Münich, on November 17, 1909, addressed the Medical Society of Münich on the topic, "Welche Mittelschulvorbildung ist für das Studium der Medizin wünschenswerth?" The address and the discussion appears in the Münchener medizinischen Wochenschrift, 1910, No. 19. To make it accessible to a larger circle of readers it has been published in 1911 in phamphlet form by B. G. Teubner in Leipzig. I quote from it the following:

"If, therefore, physics is to be taught in our universities in such a way as the physicians shall need it later in life, an absolutely different fundamental view must be taken, and this is possible

[16] Allgemeine Lehre von den Knochenbrüchen, Leipzig, 1913.
[17] Die Kinematik organischer Gelenke, Braunschweig, 1907.

only when a higher degree of mathematical knowledge is assumed. Today, not only for the study of physics, but also for the study of chemistry and physiology, a thorough mathematical knowledge is necessary. Physical chemistry which has found numerous applications in medicine and which has become indispensible in our laboratories, assumes a knowledge of higher mathematics. The text-book on physical chemistry by Nernst is for this reason unintelligible to me and, indeed, to most of my pupils. For the same reason I can follow only in part even the text-book for physicians on osmotic pressure and the theory of iones written by Hamburger. There are many students of medicine to whom the important works of Otto Frank on the problems of the circulation of the blood are only in part intelligible, because they presuppose a knowledge of higher mathematics."

During the last few years a great advance has taken place in the x-ray treatment of gynecological diseases and deep cancers, so-called deep treatment. This was made possible by inventing exact instruments for measuring the penetration and the dosage of administered rays. These instruments owe their inception to Calculus.[18]

Christen's results in the x-ray treatment relating to high penetration by hard tubes, which he has obtained by means of higher mathematics, have been verified by the practical and experimental work of the radiologists and gynecologists.

The invention and the improvement of some of the instruments used in diagnosis like the manometer, sphygmograph, etc., has been helped by the Calculus and even by its most advanced branches (Differential Equations).

It is an unfortunate peculiarity of the science of mathematics that, while a fair knowledge of one of its special branches might enable the student to follow intelligently the solutions of the simpler problems in this branch, yet even an intimate knowledge of that branch might not enable him to understand in the least degree the results in another branch. The ideas represented by the one branch and the symbolism in which these ideas are expressed are wholly different from the ideas and symbolism of another branch. On that account a specific example illustrating the application of mathematics to any branch of science can only be followed by those who have a knowledge of this branch of mathematics. Those readers who are familiar with the processes of Calculus are referred to the books and articles on the Medical Sciences named below, in which Calculus is applied. These together with the books and articles mentioned in this paper are those to

[18] Th. Christen, Messung und Dosierung der Röntgenstrahlen, Ergänsungsband 28 of the Fortschritte auf dem Gebiete der Röntgenstrahlen, Hamburg, 1913.

which I had access and the list, therefore, is quite necessarily limited.[19]

There are investigators in the medical sciences whose work involve principles of mechanics, which in turn are based on mathematical analysis. To this class of investigators belong I. Traube, of Charlottenburg, M. Ascoli, of Pavia, A. E. Taylor, of Philadelphia, H. Zuppinger, of Basel, L. Bürker, of Tübingen, L. Asher, of Bern, S. Garten, of Leipzig, H. Sellheim, of Freiburg, E. Münzer, of Prag, R. Tigerstedt, of Helsingfors, Ch. Bouchard, of Paris, R. Höber, of Kiel.

How Professor Traube has been helped by the results of physical mathematical investigations in his work on the relation of surface-tension to osmosis, digestion, narcosis, hemolysis, serodiagnosis, etc., may be judged from the following statement made by him:[20] "I attribute the clarification of my views to the fact that my attention was called to an important theorem of which I had not previously been aware, the thermodynamic demonstration of which is originally due to the great mathematical physicist Willard Gibbs."

[19] Th. Christen, Neue Wege in der Pulsdiagnostik, Zeitschrift für klinische Medisin, Vol. 71, 1910, pp. 390 to 401.

O. Frank, Endliche Ausbauchungen einer aufgespannten elastischen Membran, Zeitschr. für Biol., Vol. 50, 1908, p. 281.

S. A. Arrhenius, Immunochemistry, 1907.

K. Hürthle, Experimentalkritk der Frank'schen Theorie der elastischen Manometer, Pflüger's Archiv, Vol. 137, 1910–11, p. 153.

C. Schaefer, ibid., pp. 250 to 258.

J. Wolff, Ueber die normale und pathalogische Architectur der Knochen., Arch. Path., Anat., Physiol., 1901.

W. B. Hardy, Physiological articles in the Proceedings of the Royal Society, Vols. 86–88, 1911–1913.

O. Fischer, Physiologische Mechanik, in Encyklopaedie der Mathematischen Wissenschaften, Vol. IV, I, II, Heft I, 62 to 126, Leipzig, 1904. The index on the literature of the subject contains a list of 21 text-books and treatises and 421 monographs.

O. Frank, Prinsipien der graphischen Registrierung, Zeitschrift für Biologie, Vol. 53, 1910, pp. 429 to 456.

Th. Christen, Ueber die Anwedung zweier physikalischer Gesetze auf den Blutkreislauf, Zeitschrift für experimentelle Pathologie und Therapie, Vol. VII, 1910, p. 783.

O. Frank, Kritik der elastichen Manometer, Zeitschrift für Biologie, Vol. 54, 1903, p. 445.

K. Hürthle, Betrachtungen über die theoretischen und praktischen Bestrebungen, Instrumente sur Registrierung der im Kreislauf auftretenden Druckschwankungen hersustellen. Pflüger's Archiv für die gesammte Physiologie, Vol. 137, 1911, pp. 145 to 152.

O. Frank, Dynamik der Membranmanometer und der Lufttransmission, Zeitschrift für Biologie, Vol. 50, 1908, p. 309.

I. Petter, Die Leistungen des Sphygmographen. Zeitschrift für Biologie, Vol. 51, 1908, p. 335.

O. Frank, Prinsipien der Konstruktion von Schreibhebeln, Zeitschrift füf Biologie, Vol. 45, 1904, p. 480.

H. von Recklinghausen: Was wir durch die Pulsdruckkurve and durch Pulsdruckamplitude über den grossen Kreislauf erfahren, Archiv für experimentelle Pathologie und Pharmakologie, Vol. 56, p. 1.

Th. Christen, Die Pulsdiagnostik auf mathematisch-physikalischer Grundlage, Zeitschrift für experimentelle Pathologie und Therapie, Vol. VI, 1909, pp. 125 to 170.

H. J. Hamburger, Osmotischer Druck und Ionenlehre in den medisinschen Wissenschaften, 3 Vols., 1902–04.

[20] Pflüger's Archiv, Vol. 132, 1910, p. 511.

The great progress of the technical sciences during the last few decades is to a large extent due to the support it has received from mathematics. No one is taking up the study of the technical sciences without a more or less extended mathematical equipment. But to the study and investigation of the medical sciences, so far only a few have brought a deeper mathematical knowledge, and it is, therefore, the more surprising to learn how these few representatives have in a comparatively short time done so much toward advancing the medical sciences along mathematical lines. It augors well for the adaptability of the medical sciences to mathematical interpretation and investigation and encourages the hope that, with the increase in the number of investigators with mathematical training and ability, a more intimate knowledge of the organic laws governing the human body will be obtained and a corresponding increase in the efficiency of the methods for curing its ailments will result. While there is no medical school in this country or in Europe, which, as far as I could find, requires of its medical students a knowledge of the Calculus, there are many universities in Europe in which a course in Calculus is offered for natural science and medical students. In the Department of Chemistry in the University of Pennsylvania a few years ago a course in Calculus was made obligatory with all students.

The rapid increase during the last few decades in things material which has brought about abrupt changes in all aspects of life, is pressing also for sweeping changes in the fundamental principles of education. There is a tendency to reduce both in school and college, the amount of required mathematics. It is a fortunate circumstance, however, that we have among us men of high educational ideals with a knowledge of the past and a clear understanding of the requirements of the future, who are stemming the tide and saving as much as possible of our educational heritage, until an adjustment of the new conditions will bring those who are carried with the current to the realization and to a sober view of what comprises true education, true progress, and true happiness. The Provost of the University of Pennsylvania, with a deep knowledge of the history of the sciences and of his own specialty, an ardent investigator, with broad sympathies for the needs of those who are to be leaders, is in favor of a curriculum for a liberal education to include a thorough course in mathematics and in the ancient languages. While mathematics still possesses the educational powers as it did at that time of Gauss who found the main charm of the science in its *utter inutility*, it has during the last few decades turned into a subject of *indispensable utility*, not only in the study of the technical sciences, but also in the study of the natural and allied sciences.

A CLINICAL NOTE ON FIBROMA MOLLUSCUM GRAVIDARUM.

By Richard L. Sutton, M.D.,

ASSISTANT SURGEON, UNITED STATES NAVY, RETIRED; ASSOCIATE PROFESSOR OF DERMATOLOGY, UNIVERSITY OF KANSAS; DERMATOLOGIST TO THE BELL MEMORIAL, SWEDISH, AND WESLEY HOSPITALS, KANSAS CITY, MO.

In 1906, Brickner,[1] described an unusual type of fibroma molluscum in which the lesions developed during early pregnancy and disappeared spontaneoulsy, without scarring, a few weeks after delivery. Brickner's conclusions were based on a study of nine cases of the disorder. One of his patients had had acne vulgaris and one molluscum contagiosum; the cutaneous histories of the other seven were negative. The eruption, which consisted of forty or more small, pigmented or non-pigmented sessile or pedunculated tumors, was asymmetrically distributed over the neck and chest, and the individual lesions were apparently clinically and histologically identical with those found in an ordinary case of fibroma molluscum. The tumors varied in size from a pinhead to a split pea, and gave rise to no subjective symptoms. There was no evidence of thyroid change, and the blood and urine were normal. Brickner considered the disorder as probably metabolic in origin, and suggested for it the name of fibroma molluscum gravidarum.

DeLee[2] reported a well-defined example of the disease to the Chicago Gynecological Society, in 1908, and Goth's[3] case also was probably one of this disorder. Both Buhlig, who examined one of the tumors from DeLee's patient, and Goth found the lesions to be supplied with unusually large numbers of bloodvessels, the tumors differing in this respect from those described by Brickner.

In 1911, Hirst[4] reported a case of fibroma molluscum in a woman, aged thirty-eight years, a VII-para, in which the tumors had increased in number with each succeeding pregnancy, but had failed to disappear during parturition.

Ward's[5] patient, who was afflicted with "multiple warts in pregnancy," probably suffered from Brickner's disease, if one may intelligently judge from the meager description given.

Recently, Brickner[6] in a second communication, added seven more cases to those already reported, and also briefly reviewed some of the contributions of other writers on the subject.

Although small tumors similar to those described by Brickner are not unusual in women who have borne children, I have en-

[1] Amer. Jour. Obst., 1906, p. 191.
[2] Monats. f. Geburts. u. Gynäk., 1908, xxviii, 423.
[3] Surg., Gynec., and Obst., 1908, p. 204.
[4] Amer. Jour. Obst., 1911, p. 256.
[5] Amer. Jour. Dermat., 1912, p. 240.
[6] British Jour. Dermat., 1913, p. 153.

countered but one case in which the growths followed the characteristic clinical course of fibroma molluscum gravidarum.

The patient was a housewife, aged thirty-eight years, a native of Illinois, and a resident of Galva, Kansas. She was referred to me through the courtesy of Dr. Arthur E. Hertzler, of this city, who had been consulted regarding her condition by the family physician, Dr. Loius A. Bradbury, of Galva.

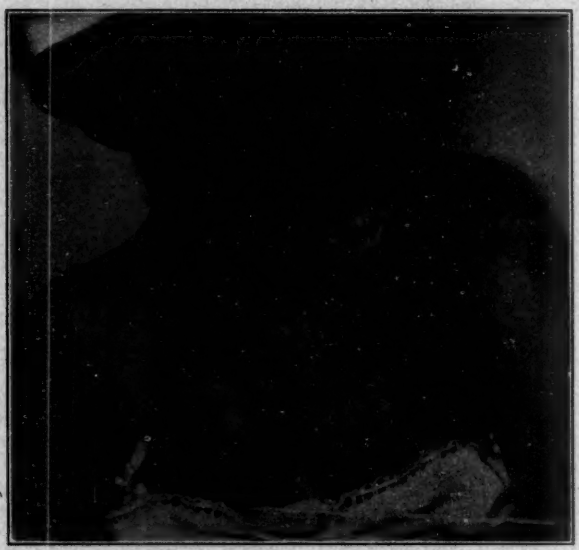


FIG. 1.—Fibroma molluscum gravidarum (case here reported).

The cutaneous history of the family was negative. The patient was a brunette, with a smooth, olive skin, and brown hair and eyes. In intelligence she was above the average, a somewhat unusual occurrence in individuals having well-marked cases of fibroma molluscum. She was the mother of two children, one three years of age and the other fourteen months. Early in her first pregnancy a number, twenty or more, of small, brown pigmented, pedunculated tumors suddenly appeared on her chest and neck. Only the mammary, supramammary, and anterior cervical regions were involved, and the growths gave rise to no subjective symptoms. Shortly after delivery the growths shrivelled and decreased in size, and in the course of three months completely disappeared, leaving no trace. During the second pregnancy another crop of the little tumors developed, some of the lesions being of considerable size, as large or larger than a split pea, and all more or less pigmented. After parturition a few of them

disappeared, but many did not, and it was for relief from those that persisted that advice was sought.

FIG 2.—Fibroma molluscum of the usual type. The majority of the tumors have been present since the patient's boyhood.

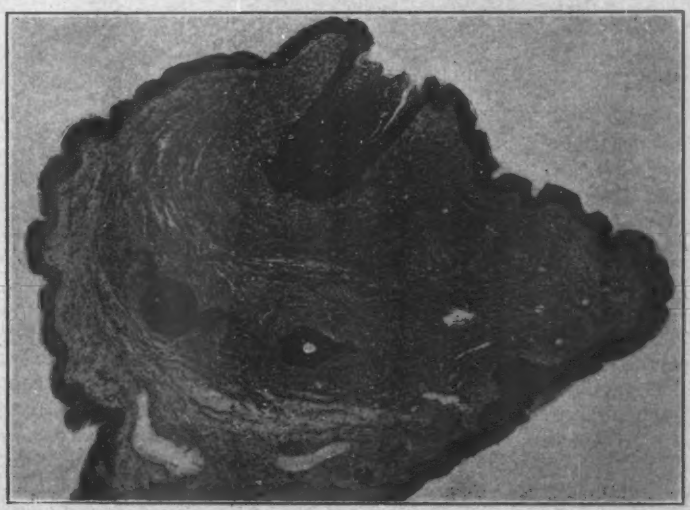


FIG. 3.—Fibroma molluscum of the usual type. Lesion from the case here shown.

A thorough physical examination revealed nothing abnormal with regard to the internal organs. Scattered irregularly over the anterior surface of the chest and neck were a number of the small, round or oval, smooth, soft, pigmented growths characteristic of fibroma molluscum. In addition to these tumors of the usual type there were a half-hundred or more minute, teat-like projections of skin which the patient stated marked the sites of former pedunculated growths, the mushroom-like tops of which had shrivelled and dropped off during the past year. For microscopic study one of the medium-sized tumors, about the diameter of a grain of wheat, was excised under cocain anesthesia, fixed in formalin solution, mounted in celloidin, sectioned, and stained by the usual methods. The stratum corneum was unchanged.

FIG. 4.—Fibroma molluscum gravidarum, showing bloodvessels and newly formed connective tissue in corium, anemic layer, which represents old corium, in papillary and subpapillary regions, and atrophy and pigmentation of rete (moderate magnification).

The granular layer averaged two cells in depth, and the elements were well preserved. The rete was decreased in thickness, deeply pigmented, and the component cells stained deeply and unevenly. The papillæ were flattened and the intrapapillary vessels were much diminished in size. The new growth occupied the centre of the tumor, and consisted of newly formed connective tissue, with its accompanying nerves and capillaries. Overlying this central mass, and separating it from the epidermis was a thin stratum of old connective tissue, anemic from pressure, and com-

paratively free from nuclei. In the vicintiy of the dividing line the lymphatics were widely dilated. No mast cells of the type described by Unna[7] as occurring in neurofibromas[8] were found. Histologically the tumor was almost a duplicate of the one examined by Goth[9].

CONCLUSION. The lesions of fibroma molluscum gravidarum are histologically identical with those of fibroma molluscum (the neurofibromas of v. Recklinghausen). As Pusey[10] has suggested, this group of cases demonstrates the possibility of production of fibromata by systemic causes, but as to the nature of these causes we are hardly in position even to surmise.

THE METABOLISM, PREVENTION, AND SUCCESSFUL TREATMENT OF RHEUMATOID ARTHRITIS: SECOND CONTRIBUTION.

BY RALPH PEMBERTON, M.S., M.D.,

PHYSICIAN TO THE HOSPITAL AND DIRECTOR OF THE DEPARTMENT OF CLINICAL CHEMISTRY IN THE PATHOLOGICAL LABORATORY, PRESBYTERIAN HOSPITAL, PHILADELPHIA.

(Concluded from February, 1914.)

TESTS OF KIDNEY ELIMINATION BY MEANS OF PHENOL-SULPHONEPHTHALEIN.

The tests below were conducted according to the accepted technique of Rowntree and Gerarghty, and need no description here.

CASE VII.—December 22, 1912. First appearance of the drug in four and a half minutes.

At the end of the first hour the elimination was	53.07 per cent.
At the end of the second hour the elimination was	13.72 "
Total elimination was	66.79 "

CASE VIII.—First appearance of the drug in nine minutes.

EXPERIMENT 1.

At the end of the first hour the elimination was	45.00 per cent.
At the end of the second hour it was too dilute to be read	

First appearance of the drug in five minutes.

[7] Histopathology of the Diseases of the Skin, Walker's translation, New York, 1896, p. 847.
[8] See v. Recklinghausen, Ueber die multiplen Fibrome der Haut, und ihre beziehung zu dem multiplen Neuromen, Berlin, 1882.
[9] Loc. cit.
[10] Principles and Practice of Dermatology, New York, 1911, p. 863.

EXPERIMENT 2.

At the end of the first hour the elimination was	40.32	per cent.
At the end of the second hour the elimination was	15.00	"
Total elimination was	55.32	"

CASE IX.—First appearance of the drug in ten minutes.

At the end of the first hour the elimination was	37.40	per cent.
At the end of the second hour the elimination was	23.80	"
Total elimination was	61.20	"

CASE XI.—First appearance of the drug in seven minutes.

EXPERIMENT 1, MARCH 25, 1913.

At the end of the first hour the elimination was	31.25	per cent.
At the end of the second hour the elimination was	13.22	"
Total elimination was	44.47	"

First appearance of the drug in eight minutes.

EXPERIMENT 2, MARCH 27, 1913.

At the end of the first hour the elimination was	33.50	per cent.
At the end of the second hour the elimination was	11.80	"
Total elimination was	45.30	"

CASE XIII.—First appearance of the drug in eleven minutes.

EXPERIMENT 1.

At the end of the first hour the elimination was	36.10	per cent.
At the end of the second hour the elimination was	10.20	"
Total elimination was	46.30	"

First appearance of the drug in eight minutes.

EXPERIMENT 2, APRIL 19, 1913.

At the end of the first hour the elimination was	43.00	per cent.
At the end of the second hour the elimination was	7.30	"
Total elimination was	50.30	"

CASE XIX.—Referred by Dr. F. H. Klaer. This patient's condition was far advanced and he was definitely crippled. The disease was of many years' standing. He was not treated, as he refused to be put on a diet, and left the hospital. It is interesting to note that in the search for foci of infection, this man had had his tonsils and adenoids removed and so many carious teeth pulled that he could eat only liquid and semiliquid diet. No relief followed. Unfortunately, the actual figures of kidney elimination were mislaid, but they were entirely normal on two separate occasions.

CASE XII.—First appearance of the drug in seven minutes.

At the end of the first hour the elimination was	53.00 per cent.
At the end of the second hour the elimination was	9.40 "
Total elimination was	62.40 "

A consideration of the above elimination figures shows that a patient with well-advanced rheumatoid arthritis may have normal elimination and that in no case tested was it distinctly low.

Case XI presented about 32 per cent. elimination at the end of the first hour, but this was no great departure from the normal for her age, which was forty-seven years.

ANAPHYLACTIC EXPERIMENTS.—The joint pains and certain other analogies between rheumatoid arthritis and occasional symptoms of anaphylaxis suggested the possibility that rheumatoid arthritis might be caused by some such mechanism, and experiments along this line were undertaken.

In view also of the demonstrable relation to the disease of proteids and carbohydrates, there was suggested the possibility of the passage through the bowel, in insufficiently altered state, of some of the elements of the proteid molecule of either animal or vegetable source.

If demonstrated the deleterious action of some of the carbohydrate foods, such as rice and potato, could be explained in part on this basis, as some workers have shown that animals can be sensitized to vegetable proteid by being fed therewith.

As a starting point, Case VII, Case VIII, Case XI, and Case XIII were respectively fed two to three soft-cooked eggs (not boiled) on an empty stomach. Two hours later about 200 c.c. blood were withdrawn from a vein of the arm under aseptic precautions and whipped. The resulting supernatent fluid was centrifuged until fairly clear and then injected in various amounts from 2 to 5 c.c. into the peritoneal cavities of guinea-pigs. In the case of Case XI the blood was withdrawn twenty-four hours after ingestion of the eggs.

At a period more than three weeks later these pigs were injected with varying amounts, from 2 to 5 c.c. of a 25 per cent. solution of egg albumen into the jugular vein or (twice) into the peritoneal cavity.

In the presence of heterologous proteid in the circulating blood of the patients fed upon uncooked eggs the guinea-pigs should have become sensitized to this, and should have shown this sensitization by anaphylaxis when injected with egg albumen. No clear anaphylactic phenomena could be detected, however, in any of the pigs.

Thinking that faulty technique on the writer's part, in giving the anaphylactic injections might be responsible for some of the first negative results, the experiments were continued with the help

of Dr. Richard M. Pearce,[1] to whom obligation is due for this and other courtesies. The results of these experiments were also negative, however.

March 10, 1913. 2 P. M. Case VII was given two soft-cooked eggs. Blood was withdrawn from the left arm at 4 P.M. After whipping and centrifuging, 2 c.c. were injected into one pig and 3.5 c.c. into another. Both these pigs were tested, with the help of Dr. Pearce, on April 8, each getting from 3.5 c.c. to 5 c.c. egg albumen solution, with negative results, as above noted.

March 11, The same experiment was performed on Case VIII, who received three raw eggs at 2 P.M. Blood was withdrawn at 4.30 P.M., and 2 c.c. were injected into the abdominal cavities of each of three pigs. One pig died April 2.

April 3. The remaining two pigs were injected intraperitoneally with 5 and 10 c.c. of 25 per cent. egg albumen solution, with no obvious anaphylactic result, one dying thirty-six hours later. The other was tested again by Dr. Pearce on April 8, as above noted, with no result.

March 30. Case XI. Blood was withdrawn at 8 A.M. and injected into three pigs, as above described, in amounts of 3 c.c. in two pigs, and 2 c.c. in one pig. Patient had had no breakfast, and had been fed one egg twenty-four hours previously. The primary purpose of obtaining blood was for determinations of the urea and non-coagulable nitrogen content. Advantage was taken of this opportunity, however, to include experiments by means of anaphylaxis at a longer period after ingestion of egg albumen.

April 19. The above three pigs were tested with 5 c.c. of 25 per cent. egg albumen in salt solution, with entirely negative results.

May 28. At 1 P.M. Case XIII This patient was fed three soft-cooked but unboiled eggs on an empty stomach, having had no other lunch. At 4 P.M. blood was withdrawn and treated as usual. Pigs 1, 2, and 3 were sensitized intraperitoneally with 5.5, 3.5, and 5 c.c. of blood respectively. Pig 1 showed weakness of the hind legs, malaise, and diarrhea, and died in thirty-six hours. The other two were essentially inaffected by the sensitizing injections.

June 19. The two remaining pigs were injected in the jugular with 5 c.c. of 25 per cent. egg albumen salt solution. Pig 3, which had had 5 c.c. of blood as a sensitizing dose, showed no anaphylactic symptoms. Pig 2, however, which had had 3.5 c.c. of blood, showed symptoms suggestive of anaphylaxis. It kicked violently with the left hind foot, continuing this in the form of scratching movements for a few moments, and then showed great collapse. It recovered from this pretty well after five minutes, and in twenty

[1] The technique used is set forth by Richard M. Pearce, M.D., in the Retention of Foreign Proteid by the Kidney, Jour. Exper. Med., 1912, xvi, No. 3.

minutes appeared nearly normal. This was the sole instance in which anything approaching true anaphylaxis was observed. The evidence from these experiments is therefore negative, and while in apparent harmony with the negative results of the blood analyses and certain other data, it must be more extended before positive conclusions can be drawn on this point. It is to be noted that the pig showing evidences of anaphylaxis was sensitized with blood drawn later after ingestion of eggs by the patient (three hours) than in the other cases. The too early withdrawal of blood may have been the source of failure here, and is to be considered in future work. It must be confessed, however that these generally negative, results and the manifestly harmful role played in this disease by pure carbohydrate render this line of investigation of doubtful promise in this particular regard.

ANALYSES OF THE UREA AND NON-COAGULABLE NITROGEN IN THE CIRCULATING BLOOD.—There have recently been devised methods which allow of the accurate analysis of small amounts of blood for such substances as urea, uric acid, and the non-coagulable nitrogen.[2]

Folin and Denis have shown that in renal disease there are marked departures from health, the total non-coagulable nitrogen rising above the normal of about 25 mg. per 100 c.c. of blood to as high as several times that amount or even in some cases to 180 mg. per 100 c.c.

The applicability of these methods to the study of such problems as the present is obvious. An attempt was made to utilize them and analyze the blood of patients with chronic joint disease: (1) to determine any abnormality in the percentage of urea and non-coagulable nitrogen; and (2) to contrast these analyses made during disease with those made after the institution of treatment and convalescence. It was conceivable that though total analyses of ill patients might show no great departure from normal, comparisons made as just indicated might show relative variations of interest. 10 c.c. of blood were withdrawn from a series of cases, as noted, at about 8.30 A.M., before the patients had had breakfast, to avoid the disturbing influences of digestion. This blood was then promptly injected into acetone-free methyl alcohol and treated according to the technique recommended by Folin and Denis.[3]

[2] New Methods for a Determination of the Total and Non-protein Nitrogen, Urea, and Ammonia in the Blood, by Otto Folin and W. Denis, Jour. Biol. Chem., June, 1912, xi, No. 5.

[3] These analyses were made by Dr. C. B. Farr and Dr. J. H. Austin, who were conducting analogous observations in connection with nephritis and desired samples of normal and pathological blood as controls for their own series. They kindly included the writer's cases among their own careful observations. A duplication of the requisite apparatus and technique seemed unwise until some preliminary observations had indicated its justification, and the writer wishes to express his thanks and appreciation to Drs. Farr and Austin for this courtesy. The Non-protein Nitrogen of the Blood in Nephritis and Allied Conditions, by C. B. Farr and J. H. Austin, Jour. Med. Research, August 1, 1912, xviii, No. 2.

The figures yielded were as follows:

	Total non-coagulable nitrogen in mg. per 100 c.c. blood.			Urea in mg. per 100 c.c. blood.		
			Average.			Average.
Case VIII, patient ill	20.2	21.7	21.0	11.2	12.6	11.9
Case IX. Experiment 1. Patient ill.	37.8	25.7	26.0	14.7	14.5	14.6
Case XI, patient ill	22.6	22.7	22.65	9.3	10.2	9.6
Case IX. Experiment 2. Patient convalescent	27.0	26.4	26.7	12.8	..[4]	12.8
Case XIII, patient ill	24.6	25.5	25.0	12.0	14.2	13.1
Case XII, patient ill	24.4	25.0	24.7	10.4	..[4]	10.4

The nitrogen of strictly normal cases averages from 20 to 30 mg. per 100 c.c. blood. The urea figures in strictly normal cases are usually about 50 to 60 per cent. of those for nitrogen, but in disease this percentage runs higher. The urea figures include the preformed NH_3 of the blood, and constitute the so-called ammonia-urea fraction. These results are remarkedly close together, and correspond to those found by Folin in perfectly healthy students. General hospital cases without nephritis show much greater variations, the total nitrogen frequently ranging up to 35 and occasionally to 40 or even more. Nephritis cases have been found usually to range above 40 and in some cases, as mentioned, to 180 mg. per 100 c.c. blood.

These figures apparently indicate that the limit of toleration to proteid in rheumatoid arthritis is not due to any "backing up" of nitrogenous matter in the blood. It will be noted that in Case IX there was no important difference between the analyses made during disease and those made during convalescence, both being well within normal limits. Further observations on this point are pending.

These observations are not without significance, as the methods used permit of an accuracy greater than has been previously attainable, and suggest that there is no important change in these blood elements during this disease. Any abnormality present, however, may be too subtle to admit of estimation, and may act by anaphylaxis or some other imponderable means. It is also conceivable that such an abnormality though present in the blood sufficiently to produce and perpetuate the disease may disappear from the blood after a night's fast.

These are more or less theoretical objections, but they should be examined.

The writer was interested to learn from the joint work of Folin, Denis, Fitz and Frothingham[5] that in experimental uranium nephritis of rabbits the phenol-sulphone-phthalein excretion agreed

[4] Duplicates bad.

[5] Fifth Annual Meeting of the American Society for the Advancement of Clinical Investigation, Washington, D. C., May 5, 1913.

with the non-protein nitrogen retention in the blood in that when the former was low, the latter was high and *vice versa*. This corroborates the writer's observations, in which the elimination by the kidney was high and the retention of non-coagulable nitrogen in the blood was low, with the molecular concentration of the urine as shown by Δ also in accord.

Attempts were also made to test the carbohydrate tolerance of these patients in respect to the glycolytic function, and a series of them was fed 100 to 150 grams of glucose on empty stomachs at 8 A.M. The twenty-four hour urines of the respective periods were collected and analyzed for sugar, with negative results. It is plain that the lowered carbohydrate tolerance of these patients is of a nature different from that characteristic of diabetes.

DISCUSSION. A consideration of the observations adduced in this series of cases permits of certain general conclusions and develops a number of points of interest.

In the first place there seems to be no reasonable doubt that the disease rheumatoid arthritis, for which a host of therapeutic measures but no successful therapy has been heretofore advanced except that directed toward a focus of infection, is in most cases amenable to treatment and can apparently be prevented. Apart from the bony changes resulting from long standing disease, and in the sense that the inflammatory process causative of them may be arrested, it seems justifiable to say that in many cases which have not responded to other treatment or to attempts to remove foci of infection the disease is curable. It should be borne in mind that the consequences of long-standing arthritis are so far-reaching that related functions often become perverted, and there may ensue a trail of complications which masks or prevents the best end-results, just as in advanced diabetes, severe or long-standing cases may eventually get beyond practicable metabolic control.

In this series of 17 cases, representing practically all varieties of the disease, none failed to improve and only 3 stopped short of a gratifying convalescence. In the light of later experience it is fair to conclude that in 2 of these cases (Case II and Case IV), which incidentally were well-advanced, the principles of treatment were not pushed far enough. It became later evident that each case was a law unto itself, with a definite metabolic limit of food tolerance which must be reached by reduction before complete results could be achieved. For clinical purposes at least the disease seems to belong in the category with gout and diabetes, in that on the one hand the proteids and on the other hand the carbohydrates can be tolerated and metabolized in certain amounts only. The analogy to gout is not quite complete, since it is the purins more especially which are at fault in the former disease, but it serves as an illustration.

The role of the fats is not quite so clear, though it seems from the experiments made in connection with Case VII and Case XII that they can be borne and successfully used to fatten those individuals whose reduction of food intake has caused much loss of weight. In any event, they are dietetically less important than the carbohydrates and proteids, but their real limit will be considered in later studies. Until further observation and wider experience develop the limitations and possibilities of the measures here outlined, each case must be carefully scrutinized and guarded. Radical changes in diet may be causative of harm unless intelligently watched, and the author urges that no case be treated heedlessly. The issue cannot be forced, and time is required for recovery under even the most favorable circumstances.

The general metabolic limit of tolerance above described may help to explain the greater frequency of the disease in women. Of 21 cases under observation by the writer only 5 were in men.

With the known greater demand which physical activity puts upon caloric intake it is conceivable that men should, as a class, be better able to metabolize a possible surfeit than would women, whose lives are as a whole more sedentary; this is only an hypothesis, however.

Comment should be made on the frequent sensation of well-being which some patients experienced when placed upon the above diets. This was noted in Cases I, V, VI, VII, XIV, XV, and XVIII (the last is not here reported).

The writer does not wish to be interpreted as asserting that rheumatoid arthritis is a purely metabolic disease, since this has not been proved. The weak link in the metabolic chain, if present, has not been found any more than it has in gout, or in some cases of diabetes, but for clinical purposes at least this conception is useful.

Among the interesting points developed in the present series in this connection is the relation of a focus of infection to the incidence and perpetuation of chronic joint disease.

Practically the only real development recently made in the therapeutics of this condition is in the recognition, removal, and vaccine treatment of such foci, steps which have restored many cases to health. Some careful clinicians believe that all cases are due to an infective focus, known or unknown.

If this be true, it places many instances of the disease in the class of those having a hidden and unrecognizable focus, since the examples are legion in which no infection can be found. Many of the present series who responded well to treatment had been searched for years in this connection without success. Therefore it follows either that there is a distinct type of the disease which is due to an error of metabolism or else that cases having a causative but hidden source of infection respond to dietary measures. This last seems unlikely, except in the sense below described.

The evidence here submitted, therefore, substantiates the views of many observers that in a large number of these sufferers the disease is due to an error of metabolism in the widest sense of the word.

In point of fact, as noted in their case histories, Case XI and Case XIII had obvious sources of infection, but notwithstanding this they responded well to dietary treatment.

A logical view of these conditions is that the metabolism in a broad sense is primarily at fault.

In certain of them there may be an unstable metabolic equilibrium which is upset by an intercurrent infection, and the disease thus induced just as a diabetic in relative health may be precipitated into coma and death by bronchitis or la grippe.

The writer makes no postulates on this score and strongly advocates the removal of infection when possible. The fact remains, however, that many cases incurable by attempts to find and remove infection may be returned to health by the above means.

A question which has long interested students of arthritis is the relations and nature of the two generally recognized types, atrophic and hypertrophic arthritis.

There are many clinical and pathological classifications of the disease, and most writers add to the above one or two more, but atrophy and hypertrophy of the joint structures, singly or together, characterize practically all cases of long standing.

In the preliminary *x*-ray studies of the cases here reported attention was given to this, and while the atrophic process generally predominated, it was practically always accompanied by hypertrophy in greater or less degree.

Inasmuch as both types responded well to the same treatment, it would seem that atrophic and hypertrophic arthritis have much in common etiologically, or are perhaps manifestations of the same process.

The writer has endeavored to formulate some rule or working hypothesis for reducing the food intake in treating these cases, based on the caloric tolerance per pound or kilo of body weight, but has as yet been unable to do so. In general, the recent cases, especially in young subjects, recover upon a larger intake than do those of long standing, so that but little modification may be required to obtain results. The duration of the disease, however, is not necessarily a criterion as to its severity or the difficulty of arresting it (compare Cases VII and Case VIII) but it is important to begin treatment early to obviate the deformities and incidental evils which otherwise result. The writer has found it useful to observe for upward of a week the normal food intake of a given case, from which the caloric level can be approximated. From this as a basis the new diet can be constructed. It is obvious that in a mild case accustomed to a high metabolic level the food intake

need not be reduced to the point necessary where the reverse is true; at least not until trial has shown this to be necessary.

Those cases presenting some soft tissue swelling as well as joint involvement are generally easier of treatment because progress can be observed in the subsidence of tumefaction and the wrinkling of the skin as well as in freer joint motility; whereas those cases presenting chiefly erosions or overgrowth of the non-articular parts of the bones may present little objective evidences of improvement. The subjective evidence of the patient over a considerable period of time, together with the loss of tenderness and limitation in movement, affords the indices in these instances.

A point which requires emphasis is that of the associated tendinous contracture and apparent ankylosis. When the activity of the arthritis *per se* has largely subsided there may come a point when the case seems to "hang fire." This occurred several times in the author's series, and was the source of considerable worry until the independent nature of the trouble was appreciated. It is of course common knowledge that these cases present contractures such as may be seen after fractures, etc., but the extent to which these contractures may simulate the condition causing them is noteworthy. The patient rarely can differentiate the two, and only close study by the observer will reveal the facts.

The appropriate treatment of such contractures is of course orthopedic, and needs no mention here except to say that, practically speaking, this has been almost as hard a question to meet, as the alleviation of the causative arthritis itself.

The long-standing habit of sparing tender joints and the reluctance to move make these convalescent patients unaware at times, of their own potential.

If to this state be added muscular atrophy, from disuse, leaving muscular tissue insufficient to move the part, the patient's quandary can be appreciated. At this point, and indeed at any stage of the disease, the time-honored adjuvants of baking, local rest, aspirin, etc., can be occasionally used, with benefit, provided they do not mask the real progress of the case through misleading temporary effects and so suggest false conclusions.

Some of the experiences here cited indicate that there may be a greater return of function in advanced cases and in apparently ankylosed joints than would seem *a priori* possible, as Case VIII and Case XI illustrate. Certainly the ulnar deviation so characteristic of these sufferers yields markedly, as shown in Case VIII, Case XII, and others. A point to be observed is that the inflammatory exudate around inflamed joints causes a fog in the *x*-ray picture which lessens and eventually disappears during convalescence. Unfortunately this does not lend itself well to reproduction in print.

Of the various joints susceptible to involvement, it may be said

that the smaller ones, like the fingers, yield before the larger, such as the knees, which are among the last to subside and to acquire freedom of capsular and tendonous movement.

The spine seems also to be quite obdurate when much involved, though the earlier stages, as in Case VIII and Case XIII, where spondylitis was present, clear up entirely.

It should be noted that pain is a feature which may persist until convalescence has been well established, and may shift from point to point even though the process as a whole be subsiding.

In watching the clinical course of these cases and certain others, there has seemed at times to occur an associated neuritis. Because of this and other observations the writer suspects that some of the neuritides belong to this general category and can be alleviated by the same methods. This is not as yet proved, but the hypothesis is worthy of being tested in suitable cases of sciatica, circumflex neuritis, and the like. Case VI illustrated this point, as she had neuritic pains in her arms. To what extent this is true of the ocular manifestations of so-called chronic rheumatism cannot yet be stated, though here again some evidence at hand is suggestive, and a trial should be made.

The relation of acute inflammatory rheumatism to the condition here discussed is interesting and undetermined. The present conception of acute rheumatism is that it is an infectious disease. Whether any other variety exists is not known, but some of the present series manifested phenomena suggestively close, clinically, to the acute form, and the writer has observed at least one case apparently of this type in which the present methods were productive of unusual results. The evidence now at hand seems insufficient for more than hypothesis, but there is at least ground for suspicion that the relation of acute inflammatory rheumatism to chronic rheumatoid arthritis may be in some cases closer than has been thought. This is being made the subject of further investigation.

Much has been written as to the etiological relation of the large bowel to this condition, and in the above cases some attention was directed to it.

Of 17 cases *x*-rayed the large bowel was elongated, tortuous, and sometimes ptosed in 14. The remaining 3 showed practically a normal position of the large bowel, but, of them, 2 were very constipated. The disease may therefore occur in persons in whom no anatomical abnormality of the large bowel can be demonstrated by the *x*-ray, as in Case II, Case XV, Case XVIII, not here included, and possibly Case XI.

Constipation seems to be a frequent though in no sense a necessary feature.

The complete role, if any, which the colon plays is not yet elucidated, though it is clear, as pointed out earlier, that proteid putrefaction within the colon is not a factor. Colonic lavage,

active purgation, sour milk dietary and other measures directed to this end, are therefore superfluous, except in so far as the general health may be benefited in other connections. Whether there may be absorbed from the colon noxious products of the break-down of both carbohydrates and proteids cannot be stated, but in any event the process is not that above discussed. The evidence to date is not in favor of the view that the disease is caused in or by the large bowel.

Attention should be called to the low number of calories upon which some of the reported cases subsisted and improved.

Case XI, Case XII, and Case XIV, after an initial fall of weight, nearly maintained an equilibrium upon about 1100 calories, a figure which is somewhat at variance with most clinical teaching as to the low limit permissible.

Sondén and Tiegerstedt, for example,[6] quote for the minimum figure for metabolism during sleep and as complete rest as possible, 24 to 25 calories per kilo, and in Case XI, here cited, they were about 20.

The above patients suffered no harm during these periods and eventually recovered, but while on the low diets were of course kept in bed. It is obvious that when it becomes necessary greatly to reduce the caloric intake of a severe case the energy output must be reduced as nearly proportionately as possible, to avoid tissue loss. The question of the calorimetry in this connection, however, is a chapter by itself, and may be made the subject of a later contribution. It should be noted that the disease began with all of these patients when they were on full diet and that during this large intake many of them developed the secondary anemia so common to this condition.

The writer is fortunate in that most of the cases cited here have been referred by other physicians, as noted in the text, who were familiar with the previous conditions of the patients or had actually treated them. Their independent observations often served as a useful control of the writer's deductions, and he owes an expression of appreciation for their interest and courtesy.

Conclusions. 1. Rheumatoid arthritis is apparently a preventable disease.

2. In most instances, except where the general health is undermined by great deformities and sequelæ of long-standing, the disease can be arrested.

3. For clinical purposes at least it seems to belong in the category with diabetes and gout, in that there is in each case a limit of toleration for carbohydrates on the one hand and proteids on the other. The role of the fats is not yet entirely clear, but they may prove to be borne analogously to the carbohydrates and proteids.

[6] Hammarsten, Physiological Chemistry, 1911, 6th ed., p. 873.

4. After arrest of the arthritis the diet can generally be gradually increased until in some cases it differs but little from that of health.

5. Both hypertrophic and atrophic arthritis respond to these measures, and their common etiology seems probable.

6. The presence of an intercurrent or possibly causative infection is not necessarily a contraindication to treatment, and recovery may take place in spite of it, though such factors should be eliminated if possible. *The large group of cases in which a causal source of infection cannot be found or removed lends itself particularly to these measures.*

7. Care is necessary to determine the highest level of metabolic equilibrium at which the arthritis will subside, and at or near that point the patient should be maintained.

8. While the general health improves with the subsidence of the arthritis, and though the patients seem to acquire a toleration for a larger dietary, the general principles above described must be rigidly observed or relapse will occur.

9. The disease is apparently not due to faulty elimination through the bowels or kidneys.

10. It is clearly not due to "intestinal putrefaction" so called. There is no reason to exclude proteid in dietary treatment, except in the sense above described, and the ordinary carbohydrate foodstuffs are also clearly capable of causing the disease.

The writer is indebted for courtesies and assistance which it is difficult properly to acknowledge.

To Dr. Samuel McC. Hamill, whose generous and broad-minded support has greatly increased the opportunities for this work; to Dr. Charles W. Burr; to Dr. William E. Hughes for the use of beds in his wards and other kindnesses; to Dr. W. S. Newcomet for coöperation in the *x*-ray studies; to Dr. Richard M. Pearce for assistance and advice; to Dr. Francis O. Allen and Dr. J. E. Sweet for surgical help; to Dr. Damon B. Pfeiffer, director of the pathological laboratory, for cordial coöperation. Appreciation should also be expressed to the President and the Board of Managers of the hospital for meeting many of the writer's requests, and to Mr. G. B. Kirkbride, superintendent of the hospital, for his receptive and helpful attitude toward new problems.

REVIEWS

TRAVAUX DE CHIRURGIE ANATOMO-CLINIQUE. By HENRI HARTMANN, Professor in the Faculty of Medicine of Paris, Surgeon to the Bichat Hospital; Member of the Society of Surgery; with the collaboration of B. CUNÉO and PAUL LECÈNE, Adjunct Professors and Surgeons to the Hospitals; KÜSS, Prosector to the Faculty; DELAMARE, V. HENRY, and LEBRETON, sometime Internes in the Hospitals. Fourth Series. Urinary Passages. Pp. 472, with 132 illustrations. Paris: G. Steinheil, 1913.

SEVEN years ago we had the pleasure of reviewing in these columns the third series of these well known Anatomo-Clinical Studies by Hartmann and his pupils. That series dealt with intestinal surgery; in the present series he returns to the urinary system which was studied in the first and second series.

Hartmann has long been recognized as a remarkable man. Claimed as one of themselves by the gynecologists, his work in abdominal surgery, especially that of the stomach, is classical; while his long experience in the *Service Civiale* at the Lariboisière Hospital, has marked him as a master of the surgery of the male genito-urinary tract.

The present volume is richly illustrated, and includes a number of important monographs, as well as articles of less magnitude. Küss describes the normal anatomy of the prostate, and Cunéo discusses in most interesting manner the question of the anatomical seat of the lesion commonly called prostatic hypertrophy. The theory he supports, formulated in 1905 by Motz and Péréarnau, is that the lesion occurs not in the prostate at all, but in the suburethral glands; and that the change is truly neoplastic in character. This view is steadily gaining ground, and appears to rest on sound reasoning, though all the facts have not yet been proved. This theory renders easy of comprehension the fact of the success of the modern suprapubic operation in cases of adenomatous enlargement, and its unsuitability for cases of urinary obstruction due to other types of prostatic disease.

Hartmann describes in some detail the technique of "transvesical prostatectomy" and, with the aid of Küss, narrates at a length of 87 pages the immediate and remote results of operation in 118 cases of prostatic hypertrophy. This number includes a few cases

of suprapubic cystostomy and of the Bottini operation; 43 operations of perineal prostatectomy; and 61 transvesical operations. Of particular value are the notes of the remote results, and especially the detailed study of specimens secured post-mortem from patients who died long after operation. One cannot admire too much the scientific spirit of the authors which has prompted them to spare no pains to render the case histories as complete as possible.

Other contributions of great value, by Hartmann, are "Some Reflections *à propos* of 47 Operations for Tumors of the Bladder:" a monograph of more than sixty pages on the "Technique and Results of Operations practised on the Kidney;" and one of considerably over 100 pages on "Surgical Treatment of Renal Diseases." Shorter articles of great interest are a "Note on the Histological Lesions in the Kidney Encountered in Certain Cases of Anuria," by Lecène; on "The Presence of Lecithins in Hypernephromas," by Delamare and Lecène; a "Contribution to the Study of the Surgical Treatment of Extrophy of the Bladder," by Cunéo; on "Osseous Foreign Bodies in the Bladder, Especially Sequestra from the Pelvis or Vertebral Column," by Küss; on "Nontuberculous Abscesses of the Prostate," by Hartmann and Lavenant; and on "Gonococcic Abscess of the Prostate," by Lebreton. Nor should we omit to mention the operative statistics of the *Service Civiale* (which form a continuation of the statistics published in the Third Series) extending from 1904 to 1907, the date when Hartmann was transferred from the Lariboisière to the Bichat Hospital.

To produce such a work as this has required an immense amount of painstaking labor; but its authors, and especially Professor Hartmann, who has inspired it all, may rest well assured that this further important contribution to scientific surgery is estimated at its true value by scholarly surgeons throughout the world, and that it has alrady taken its place as one of the classics of Urology.

A. P. C. A.

PATHOLOGY, GENERAL AND SPECIAL. A MANUAL FOR STUDENTS AND PRACTITIONERS. BY JOHN STENHOUSE, M.A., B.Sc. (Edin.) M.B. (Tor.), formerly demonstrator of Pathology, University of Toronto, Toronto, Canada. Second edition, revised and enlarged; including selected list of State Board Examination Questions. Pp. 287; illustrated. Philadelphia and New York: Lea & Febiger, 1913.

THIS book is a good epitome of the vast subject of pathology. The subject is treated as pathological anatomy, while physiology and theories are omitted. By so doing the author has been able

to compress much into his work. The inclusion of hints as to theories and physiology would help the student in consulting larger books and would occupy very little space, which could be obtained by omitting the chapter on technique, a subject rather too briefly presented to warrant its retention.

The order and system used in larger books have been followed by Stenhouse but at the end of each chapter are printed a number of leading questions upon the preceeding matter. The State Board questions are at the end.

It is not quite clear why the author includes "Internal Secretions" under the endogenous intoxications, as he does not later take up their toxicity. Their absence rather than their presence is toxic.

The eye and ear are not included, one of which at least has quite as important a pathology as the skin.

On the whole, however, the book condenses the complex subject of pathology in a way that should prove highly useful to the student. H. F.

THE MEDICAL RECORD VISITING LIST FOR 1914. New York: William Wood & Co.

THIS very handy medical day book is spaced in weekly periods throughout the year and makes possible the carrying of sixty names at a time.

Into its brief compass are crowded space for memoranda of all kinds, pregnancy charts, matter on the metric system, drugs, poisons, emergencies, and a short statement of the steps necessary to insure the execution of a valid will. A. A. H.

PATHOLOGISCHE ANATOMIE: EIN LEHRBUCH FÜR STUDIERENDE UND AERZTE. By L. ASCHOFF, Prof. of Pathology, University of Freiburg, i. Br., Germany. Third Edition. Volume I: General Etiology and Pathology, pp. 811; 431 illustrations. Volume II: pp. 1040; 661 illustrations. Jena: Gustav Fischer, 1913.

THE excellence of this text-book of pathology, edited by Aschoff with the assistance of other German pathologists, is shown by the fact that the third edition has appeared within four years of the first. A comparison of the first (AMER. JOUR. MED. SCI., 1910, cxl, 281) and third editions shows that to the first volumes have been added 175 pages and 67 illustrations and to the second 225 pages and 108 illustrations. This makes both volumes of the present edition rathr bulky and unwieldly, but this slight disad-

vantage is forgotten in the general excellence of the text and the great value of the numerous illustrations, an unusually large number of which are colored. The extensive review in these pages (AMER. JOUR. MED. SCI., 1912, cxliv, 276) of the second edition, in view of the fact that no important changes have been made in the present edition, renders unnecessary detailed comment at this time. The book remains the most complete and best illustrated general treatise on pathological anatomy for the use of students and physicians, and as it is representative of the best thought of the present-day German school of pathology cannot be too highly commended. R. M. P.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Diagnosis in the Jefferson Medical College of Philadelphia, etc., Assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics, Jefferson Medical College, Philadelphia, etc. Vol. III, September, 1913. Pp. 310; 31 illustrations. Vol. IV, December, 1913. Pp. 411; 70 illustrations. Philadelphia and New York: Lea & Febiger.

THE September number of *Progressive Medicine* begins with an article on diseases of the thorax and its viscera comprising 90 pages, by William Ewart. Over one-half of this contribution is devoted to an admirable and timely discussion of pulmonary tuberculosis. The remaining pages are given over to accounts of interesting features in physical diagnosis, bronchial affections and their treatment, and cardiology and the cardiovascular system. William S. Gottheil contributes a valuable article of 54 pages on dermatology, devoting considerable space to syphilis. Obstetrics is reviewed by Edward P. Davis in an exhaustive summary of 100 pages. Pregnancy, labor, and its complications, embryotomy, and conditions in the newborn are the headings under which he describes many important subjects. The last contribution is on diseases of the nervous system. In 54 pages William G. Spiller, with characteristic care and thoroughness, takes up a large number of interesting topics.

The December number opens with a contribution of 112 pages, by Edward H. Goodman, on diseases of the digestive tract and allied organs. As usual, gastric ulcer and carcinoma claim considerable attention. Duodenal ulcer, peristalsis and antiperistalsis of the large intestine, the treatment of intestinal toxemia, hepatitis, diseases of the biliary tract, and pancreatic conditions may be noted as a few of the many topics described in this painstaking article. An excellent, but short, contribution of

19 pages by John Rose Bradford, on diseases of the kidneys is followed by a paper of some 48 pages on genito-urinary diseases by Charles W. Boney. Joseph C. Bloodgood again contributes a noteworthy review of 102 pages on the surgery of the extremities, shock, anesthesia, infections, fractures and dislocations, and tumors. The always instructive and practical discussion of therapeutic advances by H. R. M. Landis, occupies 96 pages and concludes the volume.

A survey of the four volumes of *Progressive Medicine* that appeared during 1913 makes it evident that the contributions to this useful quarterly continue each year to be of increased interest by reason of the care and excellent critical judgment displayed in their preparation. G. M. P.

MANUAL OF TROPICAL MEDICINE. By CARTELLI and CHALMERS. Second Edition. Pp. 1747; 630 illustrations. New York: William Wood & Co., 1913.

IN 1910 the first edition of this work appeared, as a result of studies upon pathological conditions occurring in tropical Africa and Asia. Additions to the first publication (which consisted of 1250 pages) will be found in almost every part of the book and yet the publishers have managed to confine this increase in matter to one, though perhaps rather bulky, volume. It would seem that a future edition would be rendered more serviceable in two volumes, with binding and paper as light as possible. Not infrequently investigators in the tropics go to distant points for study, taking their apparatus and literature. Castellani and Chalmers are the authors, yet it is evident that the most generous aid in text and illustration has been rendered these writers, in the preparation of this work. Among those who have so rendered assistance are Leishman, Ross, Nuttall, Grassi and many other authorities in tropical medicine. The worker in this field is, for the most part a philanthropic scientist and renders without stint or selfish reservation every contribution at his disposal. When, therefore, the second edition of this work appears three years after the first with additional names such as Splendore, Stephens, Brumpt, Newstead, Terni, Mesnil, MacLeod, Pittaluga and many others (34 in all) from whom "kind help" was received, we may feel that the authors have brought together the most valuable opinions obtainable to date. The work omits descriptions of practical laboratory methods and detailed descriptions of bacteria. In place of such descriptions space has been given to parasitology and treatment. Indeed the work may be considered to be, in text and illustration, a treatise on parasites and parasitic diseases. The parasites are physiologically, biologically, and anatomically con-

sidered in detail and diagnosis and treatment of the diseases they produce are dealt with at length. Treatment in general is taken up with such care and thoroughness that these chapters must be given a place among practical works on therapeutic and preventive medicine.

The chapters on tropical races and climatology and effect of food and climate on man in the tropics, present some valuable contributions to the study of the suitability of localities for settlement and of the methods of food supply and preservation.

The sections on the physical and chemical causes of disease contain much valuable information of special as well as of general interest.

Those better qualified than the present reviewer will doubtless find in the work features to adversely criticise, and time too will disclose errors and omissions, but one can not but congratulate the Profession upon obtaining in so small a space the result of so extensive an amount of research work by the world's greatest authorities.

The dedication of this, as well as the first, edition to Sir Patrick Manson, whom the authors entitle "The Founder of Scientific Tropical Medicine," is peculiarly fitting. C. N. B. C.

BLOOD PRESSURE IN GENERAL PRACTICE. By PERCIVAL NICHOLSON, M.D. Pp. 157; 7 illustrations. Philadelphia and London: J. B. Lippincott Company, 1913.

FEW subjects in medicine have attracted more widespread attention during the past decade than have studies on blood pressure and its clinical application. As a consequence a voluminous literature has rapidly accumulated and much speculation and controversy has arisen. As the result of these many observations, certain facts of great clinical importance and practical value have been established; but these facts are so scattered through the literature of a number of years that it has been well nigh impossible for many to become familiar with them. Nicholson, appreciating this situation, has been the first since Janeway's memorable book appeared in 1904, to gather together the important and well established facts that have been ascertained in reference to blood pressure. He has written a little book primarily for the general practitioner and student. He has avoided the temptation to digress into the alluring realms of the pathology and physiology of arteriosclerosis, nephritis, etc., has wisely adhered strictly to his purpose and has given us an admirable, concise account of the value and significance of blood pressure determinations in general practice.

After a few pages devoted to general considerations and defini-

tions, he describes the methods of estimating blood pressure. He emphasizes the importance of the auscultatory method, which he rightly regards as the most reliable method and the only simple one which gives accurately the diastolic pressure. Incidentally, his account of how to determine diastolic pressure is correct and in accordance with the most recent observations on this point. He also dispells some of the confusion that has arisen in regard to the inertia of mercury by pointing out that from the practical standpoint it is of little significance.

The second chapter is devoted to a discussion of various blood-pressure instruments. Although admitting the advantage of their portability, Nicholson regards the spring aneroid type of instrument as inaccurate and not dependable. At the close of this chapter, with becoming modesty, he devotes only a little over a page to a description of the admirable sphygmomanometer of his own invention, an instrument which in the hands of many has proved reliable, convenient, and in every respect satisfactory.

It is gratifying to note in a later chapter that this author lays particular stress on the importance and significance of the heretofore too much neglected diastolic pressure and pulse pressure. The subjects of hypertension and hypotension, the conditions in which they occur, and their treatment, are well considered in separate chapters. Blood pressure in surgery and anesthesia and the importance in life insurance are also taken up. A useful, though incomplete bibliography, and a careful index, conclude the book.

The book is written in a way that should make clear to the most inexperienced the fundamental principles upon which blood pressure and its determination is based. Moreover, the practical importance of the subject is pointed out so definitely that this little book should do much toward popularizing sphygmomanometry among those practitioners who have as yet failed to appreciate its inestimable value. G. M. P.

THE SURGICAL CLINICS OF JOHN B. MURPHY, M.D., AT MERCY HOSPITAL, CHICAGO. Vol. II, No. 5, October, 1913; and No. 6, December, 1913. Pp. 175 and 187, with 83 illustrations. Philadelphia and London: W. B. Saunders Company, 1913.

THESE two numbers of *Murphy's Clinics* conclude the second volume of this remarkable work. It has been a little more carefully edited than the first volume, but there still is much room for improvement. The general plan of the work remains the same, but there has been a freer use than in the first volume of clinical talks and lectures by other teachers than Dr. Murphy, himself,

thus in the October number there is a "talk on cancer" by Dr. W. L. Rodman, of Philadelphia.

Some of the editorial shortcomings may perhaps be alluded to: most notable of all; because appreciable at a glance, is the persistence of Dr. Murphy in using the barbarous phrase "osteitis fibrosa cysticus;" this jumble of Latin genders cannot be attributed to a mere typographical error, because it is so frequently repeated that Dr. Murphy evidently believes it to be correct usage. Another editorial shortcoming is failure to correct and revise crudities of diction; for example (p. 797): "Again it will be noted how the transplanted periosteum remained as a white line for seven months after the implantation, and that it was an apparent detriment to the production of bone;" (this is clear enough, of course, and inculcates an important lesson; but hear what follows): "It was finally involuted by bone formed from the periosteal zone helm at the nail upward around the new-formed callus and outside of the transplanted periosteum." Now, what on earth does all this mean?

Still another editorial shortcoming, rather amusing in its effect, is failure in some instances to harmonize premises with conclusions; for instance: Dr. Murphy is operating on a patient with a healed duodenal ulcer, in whose case no positive diagnosis had been reached before operation; he finds (p. 826) "a strangulating band extending completely across the stomach and constricting it in the pyloric zone." He comments: "All the symptoms which he has had can now be interpreted. He has had blood in his stools. He has had an ulcer here at some time which caused that constriction." Then, *mirabile dictu*, Dr. Murphy adds, a few lines further on, "He did not have a single symptom pointing to this condition." Surely only a genius like Dr. Murphy can explain all the symptoms by the pathological changes when the patient had not a single symptom which pointed to the pathological changes found.

But, all captious criticism aside, even though Dr. Murphy frequently, if unconsciously, contributes to the gaiety of nations (these Clinics are read all over the world), his contributions to surgical diagnosis and technique are of more importance, and are always gratefully received by students everywhere.

A. P. C. A.

COLLECTED PAPERS BY THE STAFF OF ST. MARY'S HOSPITAL, MAYO CLINIC, ROCHESTER, MINNESOTA, 1912. Pp. 842; 219 illustrations. Philadelphia and London: W. B. Saunders Company, 1913.

THE Mayo Clinic continues to issue, yearly, a volume replete in interest, valuable for reference, and covering increasingly

various fields of surgical activity. Surgery of the alimentary tract is gradually being overtaken by that of other departments.

Most of the papers are concerned less with operative technique and the immediate mortality of operation (as was formerly the case) than with pathogenesis, diagnosis, and ultimate results. Most of the papers, also, are comparatively short, and in the case of some of those which appear longest, closer investigation shows that most of the bulk is formed by the illustrations. Thus, MacCarty and Blackford contribute a paper of the "Involvement of Regional Lymphatic Glands in Carcinoma of the Stomach," based on a study of 200 specimens obtained at operation; 22 pages of this article are devoted to diagrams of the position of the infected lymph nodes, 5 pages to half-tone illustrations, and only 10 pages to text. C. H. Mayo discusses the "Surgery of the Single and Horseshoe Kidney" in a paper of 15 pages, of which only a little more than half is text; there are 9 figures representing the gross appearances of specimens, only two or three of which seem of real merit. Indeed, it is questionable whether it is ever worth while to publish photographic reproduction of more than a very few pathological gross specimens, since they often appear merely as ink smears even in the best reproductions.

The volume also contains many important articles which have already taken their place in surgical literature, notably those dealing with the surgery of the spleen, of the thymus gland, and on benign and malignant ovarian cysts. At the end are to be found a number of papers and addresses on topics of more or less general interest; and finally a short note on the Laying of the Corner-Stone (October 10, 1912) for the new office, laboratory, and library building in process of erection for the Mayo Clinic. Dr. Mayo said: "The object of this building is to furnish a permanent house wherein scientific investigation can be made into the cause of the diseases which afflict mankind, and wherein every effort shall be made to cure the sick and the suffering. It is the hope of the founders of this building that in its use the high ideals of the medical profession will always be maintained. Within its walls all classes of people, the poor as well as the rich, without regard to color or creed, shall be cared for without discrimination."

A. P. C. A.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

CHIEF OF THE DEPARTMENT OF INTERNAL MEDICINE, CLIFTON SPRINGS SANATORIUM AND HOSPITAL, CLIFTON SPRINGS, NEW YORK.

Acute Graves' Disease.—In reporting 4 cases of acute Graves' disease, FUNKE (*Zentralbl. f. inn. Med.*, 1913, xxxiv, 705) agrees with Schlesinger and others, that the one most characteristic symptom is tachycardia: exophthalmos and struma are often notably insignificant; other typical manifestations are marked arrhythmia, increased blood pressure, and exceedingly rapid emaciation. Fever of a remittent type is commonly seen. In all cases there was considerable splenic enlargement, intractable vomiting, and more or less continuous jerking of the entire body, reminding one of a chorea major. Dysphagia was frequently complained of. In 1 case there occurred tetany-like cramps in the hand and a positive Chvostek's sign. Jaundice was encountered, and considered to be of toxic origin as was the splenomegaly. Status lymphaticus was present in 2 cases. The usual determining cause of acute Graves' disease is some severe psychic shock. Funk advises against surgical intervention; all 4 cases had a successful outcome, though none were benefited by the use of antithyreoidin.

Functional Test of the Kidney in Uremia.—FOSTER (*Arch. Int. Med.*, 1913, xii, 452) cites three different types of nephritis for the purpose of emphasizing the importance of functional tests by themselves. The first, with cardiac hypertrophy, arterial hypertension, albuminuria and cylindruria, developed albuminuric retinitis in November. In December, the excretion of phenolsulphonephthalein was 53 per cent. Death in coma occurred suddenly in February after a convulsion. Section showed a red granular kidney. The second case showed no cardiac enlargement or hypertension. There was

albuminuria and cylindruria. The excretion of phenolsulphonephthalein three days before death, while the patient was in coma, amounted to 63 per cent. Section revealed a small granular kidney. The third case was characterized by anasarca, small heart, and low blood pressure, considerable albumin and many casts in the urine. Death was sudden after a convulsion. Eleven days before, the phthalein test gave 57 per cent. output. The clinical diagnosis in last case was confirmed at section. In all the phenolsulphonephthalein test gave a figure approximating normal. Yet in view of the termination of the cases, one would hardly venture to assert that the renal function was normal. As to prognosis, this test would have indicated that recovery was almost certain. Foster questions whether the excretion of this drug does not depend on some other factor than pure renal disease, which by its presence or absence determines the rate of secretion by the kidney—as circulation or non-protein nitrogen in the blood. However, the same finding occurs with incoagulable nitrogen in the blood in uremia. Foster cites a case of death from uremia with a low normal estimation of non-protein nitrogen in the blood. He warns that the consideration of such methods of investigation as ultimate criteria leads into errors of diagnosis, narrowed medicine, and false ideas as to the pathology of a disease entity.

Chemical Nature of Eosinophilic Granules.—Müller (*Wien. klin. Woch.*, 1913, 1025) found that if air-dried blood films are fixed for six hours in the incubator, submerged in a saturated aqueous solution of $K_2M_nO_4$: without washing, then stained for several hours in Kultschitzky's hematoxylin solution and finally counterstained with Weigert's borax-ferrocyanide mixture until the red-blood cells are colorless, and the white cells appear as bright gray disks the esinophilic granules then appear as brown or blue-black dots. After the action of various lipoid solvents the granules will no longer stain black in the above method, though they retain their affinity for acid aniline dyes. This affinity is probably due to a protein complex—as demonstrated by Petry; but besides this, the granules probably are made up of some lipoid constituents.

On the Effect of Opiates upon Peristalsis.—E. Stierlin and N. Schapiro (*München. med. Woch.*, 1913, lix, 2714) find that the *x*-ray studies of the affects of opium and its derivatives on peristalsis in the stomach and intestines, as reported in literature, are very conflicting. They have therefore, investigated the subject on man and on animals. Patients with fistulæ of the small intestine and with cecal fistulæ, as well as normal individuals have been studied. In a dog the small intestine was divided half-way between the stomach and large bowel. The upper half was implanted in the cecum, whereas the open end of the lower half was inserted in the abdominal wall. By this means it was possible to study the affect of the drug on the stomach and small intestine separately. Stierlin and Schapiro find that morphine has a variable action on gastric peristalsis. Usually in the young, moderate doses delay the emptying of the stomach several hours, even to twice the normal time. In adults, on the other hand, this action is much less marked and less constant. In 2 cases of hyper-

motility of the stomach, the emptying was even more rapid with opium than without it. In the small intestine they found a delay of the intestinal contents under the influence of morphine amounting to as much as seven hours. Often only the lower ileum remained filled longer than the normal time, suggesting a contraction of the sphincter at the ileocecal opening. No alteration could be discovered in the tonus of the small intestine. Upon the large bowel, no affect was observable, opium and pantopon acting in practically the same way as morphine. In chronic diarrhea with marked hypermotility of the small and large intestine, opium produces a slight retardation in the passage of the contents in the lower part of the small intestine; no effect was found on peristalsis of the large bowel down to the sigmoid flexure. The sigmoid remained filled longer than without the morphine. The constipating effect of opiates is due not so much to retardation of peristalsis as to dulling or inhibition of central defecation reflexes and the resulting delay of the contents in the sigmoid, Stierlin and Schapiro conclude.

Diastolic Ferments in the Urine.—(*Deut. Arch. f. klin. Med.*, 1913, iii, 164.) In making determinations of the diastatic ferments in the urine, according to Wohlgemut's method, NEUMANN calls attention to the fact that reliable estimations should be based upon the twenty-four-hour output. The total diastatic ferment amount, *per deim*, varies much with the same individual, and appears to be influenced more by psychic factors than by changes in the diet. Generally the diastatic power of the blood serum is less than that of the urine. This is found to be definitely decreased in diabetes mellitus, the amount of reduction being of some prognostic value. It is also diminished in pernicious anemia, Basedow's disease and in some forms of nephritis. The notable increase in pancreatic disease, is of real diagnostic worth. There is a slight increase in urinary diastase in some febrile conditions. Investigations carried out in a number of other diseases showed no great deviation from the normal.

Experimental Pathology and Therapy of Syphilis.—UHLENHUTH and MULZER (*Arb. a. d. Kais Gesundh. Amt.*, 1913, xliv, 307) report a long and extensive series of investigations carried on in the field of experimental lues. Human luetic material was used, after numerous passages through dogs, a process which greatly increases the virulence of the spirochete and decreases the incubation time of the disease. Intravenous or intracardiac injections of such material in dogs, causes, in a high percentage of cases, generalized lues. In from six to ten weeks the animals become unkempt and lean. Soon there appear, especially in young animals, small, dark tumors about the nasal orifices, the end of the tail becomes knobby, and bean-like excrescences are common on the edges of the eyelids; these always in association with an intense conjunctivitis. These tumors, which commonly show superficial ulcerations, contain great numbers of spirochetes. Ulcerated papular syphilides may occur around the anus and vagina. In some instances the inoculation of extracts of various of the internal organs of such animals, into normal dogs, induced lues in the latter. Luetic testicles or the occurrence of eye manifestations seem to offer no protection

against further inoculations, nor do the sera of dogs, repeatedly injected with spirochetes, protect other dogs from the disease; such sera are likewise of no therapeutic value. Uhlenhuth and Mulzer were unable to cultivate the spirocheta pallidum from infected animals. With reference to transmission of the disease, it was found after intravenous injections of the spirochete, the organisms were able to penetrate the sound placenta within five minutes and could be demonstrated in the fetus. The injection of blood from individuals in the primary or secondary stage of lues, caused a specific orchitis in 78 per cent. of the cases; even the blood of persons having latent syphilis and showing a negative Wassermann reaction can be infectious. Uhlenhuth and Mulzer conclude therefore that lues is essentially a chronic septicemia.

Theory of the Wassermann Reaction.—Prausnitz and Stem (*Zentralbl. f. Bakteriol.*, 1913, lxix, 545) in going over the subject of the Wassermann reaction it was found that both aqueous and alcoholic extracts of luetic livers gave complete complement fixation in the presence of luetic sera; alcoholic extracts were much more potent and reliable; alcoholic extracts of the residue from the syphilitic livers were inactive. It was found that intravenous injections, into dogs, of either of the above potent extracts would induce a positive Wassermann reaction in their sera; controls, with normal extracts were always negative. Since experimentally the production of an active antibody results from the introduction of a substance or substances soluble in alcohol, and probably of a lipoid nature, while on the other hand only proteids induce antigen production, it seems reasonably certain that the Wassermann reaction is not a true antigen-antibody process. The reaction is to be considered characteristic when positive, but not specific. Whether the lipoids in the reaction originate from the luetic tissue or from the spirochetes, remains to be seen.

The Blood Picture in Status Lymphaticus.—Siess and Stoerk (*Wien. med. Woch.*, 1913, lxiii, 1123) give a report of 23 cases, diagnosed by reason of the following symptomatology: (1) Atypical arrangement of the hair; (2) abnormal length of the extremities; (3) scaphoid scapulæ; (4) a wide pelvis in males, narrow in women; (5) adiposity of the reverse type, in the lower half of the body in males, upper half in females; (6) poor development of the breasts; (7) general glandular hyperplasia; (8) small but elongated heart associated with a strong apex beat and an accentuated aortic second sound; (9) low blood-pressure; (10) psychoneurotic manifestations; (11) vagotonia; (12) infantile type of epiglottis. The blood findings in such cases showed few deviations from the normal picture. Thus the red-blood corpuscles varied between 3,000,000 to 5,000,000, the hemoglobin being generally high. Contrary to a general belief the white cells are not consistently low-ranging in this series from 4300 to 10,000. As regards the various white cells, the neutrophilic leukocytes, large mononuclears, and transitionals are within normal limits; lymphocytes rarely exceed 2000 per c.c. but quite characteristic of them is their unusually abundant protoplasm. Eosinophiles are consistently low, whereas the abundance of blood platelets is a noteworthy feature. Functional tests of the activity of the bone-marrow, made by means of gelatin infections,

showed an increase in neutrophilic leukocytes considerably lower than normal; on the other hand the mononuclear elements not only failed to show the customary decrease, but in 4 cases were absolutely increased.

SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

Traumatic Epilepsy and its Surgical Treatment.—MATTHIAE (*Deut. Zeitschr. f. Chir.*, 1913, cxxiii, 417) collected from the literature and studied 326 cases of traumatic epilepsy, which had been operated on. Of these 60 were of the general and 266 of the Jacksonian type. Favorable results (cure with permanent recovery or recovery lasting some years) were obtained in 96 cases, of which 81 were of the Jacksonian and 15 of the general type. The results were unfavorable (no influence, made worse, or death) in 81 cases, of which 59 were of the Jacksonian type and 22 general. The remaining cases were observed for too short a time or either the results or the time of observation were not given. The time of observation after which one can speak of a permanent cure, should be at least five years. In these 326 cases there were only 4 in which the attacks recurred after they had ceased for several years. In one they recurred after a cure of four years, in two others after five years and in the fourth after six years. The time of observation should be, therefore, at least five years. In all, 24 cases were followed for more than five years, of which 21 were of the Jacksonian and 3 of the general type. A cure (for under five years but one year at least) was obtained in 40 cases (Jacksonian 36, general 4). Improvement was obtained in 27 (Jacksonian 19, general 8). There was no improvement in 59 cases (Jacksonian 42, general 17). The condition was made worse, evidently from the operation itself, in 3 cases, and 19 died as the result of the operation (Jacksonian 16, general 3). Death was due to shock or collapse in 6 cases, meningitis in 5 cases, status epilepticus in 3 cases (one of which died as the result of tonic contraction of the diaphragm). In one case death was due to pleuropneumonia and secondary hemorrhage. The favorable cases were all observed at least one year, while in the failures the period of observation was sometimes less. According to experience up to the present time, improvement and cure may develop only a long time after operation, just as the improvement after operation may disappear again after a time.

The Operative Treatment of Prostatic Hypertrophy.—ENGELMANN (*Deut. Zeitsch. f. Chir.*, 1913, cxxiv, 116) discusses the treatment of prostatic hypertrophy by vasectomy, a suprapubic fistula of the bladder, the galvanocaustic incision of Bottini, and prostatectomy. The latter has become the operation of choice, especially the suprapubic prostatectomy. In discussing vasectomy, he says that when the gland is soft and not very large, this operation produces a diminution in the size of the gland and in the retention of urine and subjective symptoms. He employed it in about 100 cases, and obtained satisfactory results in over 50 per cent. He regards it as suitable (1) for the early stages of the affection when there is transitory but frequently repeated complete retention of urine, hemorrhage and subjective symptoms; (2) as a preliminary operation to prostatectomy or the Bottini operation in patients inclined to epididymitis; (3) when the condition of the patient forbids a severe operation. In the last group of cases, if catheterization is too difficult or impossible, he sometimes makes a suprapubic fistula in the bladder, when vasectomy fails. In the last eight years he has done 91 Bottini operations and 31 suprapubic prostatectomies. The indication for operation is always retention of urine, complete or incomplete, persisting in spite of catheterization, sounds or vasectomy. Most of his cases had cystitis, some had pyelitis or pyelonephritis, which do not contra-indicate the operation but do affect the choice of operation. The Bottini operation should not be done in patients with pyelonephritis. At first this operation was done under local anesthesia, but later lumbar anesthesia was found to be more effective. Three incisions in the gland by the galvanocaustic incisor, were employed in almost all cases. In rare cases, especially when the prostate was large, four were made. Of 90 cases thus treated 69 were cured, 10 considerably improved, 3 not improved, and 8 died. In other words, 87.8 per cent. gave good results and 12.2 per cent. were failures. Of the 90 cases, 75 suffered from cystitis and 23 from pyelitis or pyelonephritis. Of the 8 who died from the operation, 7 had chronic pyelonephritis, exacerbations of which with the associated urosepsis were responsible for 6 of the deaths. In these 31 prostatectomies, he had 6 deaths. The indications for the choice between the two operations are as follows: Prostatectomy is to be preferred when the prostate is very large and when a pedunculated middle lobe projects into the bladder. With a relatively small hypertrophy, especially if an hypertrophied middle lobe is in the form of a barrier to micturition, the Bottini operation is to be preferred. It is to be done when the prostate is very large, only when the general condition contra-indicates a prostatectomy. When there is infection of the urinary tract especially a pyelonephritis, prostatectomy gives better drainage. If the kidney function is much impaired, palliative treatment (cystostomy, vasectomy) is to be employed

---

The Pathogenesis of Hydrocele.—ZESAS (*Zentralbl. f. Chir.*, 1913, xl, 1291) says that it is already known that hydrocele is much more frequent in the warm and tropical climates than in the cold. Some writers ascribe this to a more active function of the testicle in warm countries, while others ascribe it to the direct effect of the warmth. According to the latter view the warmth produces a relaxation of the

scrotum and spermatic cord, because of which the testicle and its enveloping structures are exposed to mechanical irritation. The following case serves as an illustration of this method of origin: A young farmer was affected at every harvest time by a one-sided hydrocele, which disappeared completely in the autumn. He was advised as a prophylactic measure to wear a suspensory bandage during hard work in the warm season. This was followed by complete relief from the hydrocele. Much more frequently the hydrocele is due to infections occurring in the warm climates, particularly to malaria. In many cases operated on by Zesas, the patient had suffered or was still suffering from malaria. It was observed also that in those patients who still suffered from malaria together with the hydrocele, there were inflammatory changes in the testicle and epididymis, while in those patients who had recovered from their malaria, the testicle appeared to be normal and the hydrocele was the result of the preceding inflammatory process. Inflammations of the testicle are not very rare in malaria. During the febrile attacks swelling of the testicles and epididymes is the rule, and it is usual for the disease to be associated with a serous vaginalitis. As a rule these symptoms disappear completely from rest in bed and the administration of quinine. Occasionally atrophy of the testicle or thickening of the epididymis remain. The hydrocele appears to be a secondary manifestation of malaria and is either an accompanying symptom of malarial orchitis or epididymitis, or is the remains of such a process. Recurrence of the hydrocele after a radical operation, says Zesas, cannot be excluded with the existence of the anatomical changes in the testicle.

The X-rays in Gouty Arthritis.—JACOBSOHN (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1913, xxvi, 531) says that joint diseases due to a gouty diathesis are not always diagnosed from the non-gouty cases by the clinical manifestations. The so-called chronic rheumatism (atrophic arthritis) often shows the same clinical picture. Laboratory methods are often not available. The *x*-rays are not without value and deserve a place among the other diagnostic methods. In estimating the value of the *x*-ray examinations of gouty joints and how far they can aid in the differential diagnosis between this and other joint diseases, Jacobsohn says: Even when the diagnosis of gout is established, one or several skiagraphs should be made because they show the grade of changes in the joint by the disease. For the prognosis it is important to know whether only simple changes (bone atrophy, narrowing of the joint space) is present or the whole joint destroyed. He disagrees with Gélibert and Lumière who advise that the tophi should be removed, because by so doing one could not prevent the irregular bone changes which would later interfere with the function of the joint, and limb. Gouty arthritis can give, by the *x*-rays, signs which are peculiar to it and which, therefore, may be regarded as pathognomonic. These are the changes in the bones, which consist particularly in the deposits in the bone showing in the *x*-ray plate as transparent defects in the bone. They may be round, oval or irregular, but are present, however, in only a small percentage of the cases in which the clinical picture is only that of a chronic rheumatic arthritis (arthritis atrophicans), although they are then of much diagnostic importance.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF APPLIED THERAPEUTICS IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

Splenectomy in Treatment of Pernicious Anemia.—HIRSCHFELD and KLEMPERER (*Therapie d. Gegenwart*, 1913, liv, 385) report two cases of pernicious anemia in which marked improvement followed splenectomy. They were led to try this radical procedure by the fact that a previous patient with Banti's disease developed a pronounced polycythemia a year and a half after a splenectomy had been performed. In this patient the hemoglobin rose to over 120 per cent. and the number of red blood cells increased to seven and eight million, and the blood picture was in marked contrast to the former severe secondary anemia. In addition there are also a number of other cases on record in which a polycythemia has developed after a splenectomy for rupture of the spleen. They believe that probably pernicious anemias of recent origin will be more favorably influenced by splenectomy than cases of long standing. The most striking effect observed in the two cases reported by Hirschfeld and Klemperer was the marked and prompt increase of nucleated red blood cells in the blood. The effect produced was so striking that it showed conclusively, according to Hirschfeld and Klemperer, that the splenectomy stimulated the production of red blood cells on the part of the bone marrow. In one patient the hemoglobin rose from 30 to 55 per cent. in one month and to 80 per cent. after two months, with a corresponding increase in the number of red blood cells. Although the blood of these patients still has certain features of pernicious anemia, especially the presence of numerous megalocytes, yet the results obtained justify the conclusion that this procedure has a definite influence in stimulating the production of red cells.

The Effect of Atophan and Novatophan on the Endogenous Uric Acid Excretion of Normal Men.—HASKINS (*Jour. of Pharm. and Exper. Therapeutics*, 1913, v, 33) investigated the effect of atophan and novatophan upon the endogenous uric acid excretion in 21 normal men. All of them had been on a purin-free diet for one week before atophan or novatophan was administered. The first 16 reported in the table showed over 200 mg. increase of uric acid excreted under the influence of the drug. This increase was most marked on the day following the administration of the drug. Four others showed a less marked increase, but in 1 case the increase was not apparent until the second day. The one subject that showed no increase of uric acid was only examined on the day following the administration of the drug and Haskins suggests as an explanation that in his case the elimination might have been delayed. Judging by the results

obtained by Haskins, atophan seemed to be more efficient in its action than novatophan. Investigation, undertaken to compare the excretion of the period after taking the drug with the period before taking it, showed that the excretion of uric acid was at a distinctly lower level in the period after the administration of the drug than preceding it Haskins believes that the results of his investigations point strongly to the possibility that the main effect of atophan and novatophan is to drain uric acid out of the blood, leaving the uric acid content of the latter subnormal.

Artificial Pneumothorax in the Treatment of Chronic Infection of the Pleura and the Lungs.—FLOYD (*Boston Med. and Surg. Jour.*, 1913, clxix, 713) reported two years ago with Robinson a series of 28 cases of pulmonary tuberculosis treated by artificial pneumothorax. Of this number 8 cases had either shown an entire arrest of an active process or were approaching that condition. The remaining 20 cases had secured relief of symptoms to a greater or less degree. Of the arrested cases, six are in excellent condition at the present time. One has died, through no fault, however, of the method and one has, within the last year, shown an extension of the old process into the previously collapsed portion of the lung. Floyd says that during the past four years he has treated a large number of cases of pulmonary tuberculosis by this method. Some of these have been under treatment primarily for the relief of one or more symptoms, such as persistent cough, or hemoptysis. In the great majority, however, the object of the treatment has been to arrest an advanced active process. In the larger number of cases reduction in temperature, relief of cough, diminution of expectoration and an increase of body weight have occurred. In several cases where the character of the disease was that of a chronic toxemia with an advanced pulmonary lesion, the results of the compression of a portion of the active lung has markedly diminished toxic absorption. Improvement in circulation, gain in weight, and increase of strength followed, even where the extent of pneumothorax was limited. In one case of pyothorax secondary to an advanced tuberculous process of the lung in which the pus was withdrawn and the fluid replaced by nitrogen no results were obtained on account of the dense unyielding condition of the consolidated lung. In cases of pulmonary tuberculosis complicated with a secondary infection results have been fairly good only where collapse of the lung has been extensive. The compression of a portion of the lung tends merely to diminish the amount of sputum and reduce temperature. The action of pyogenic organisms is not checked and lung destruction slowly advances. In the unilateral cases of active tuberculosis not only relief of symptoms but arrest of the disease has been obtained. The time required to accomplish this has varied with the extent and activity of the disease. The tendency in most instances is to lengthen the interval of injections too rapidly and even stop them altogether before permanent arrest is assured. With artificial pneumothorax as with other methods of treatment of tuberculosis relapses occur and a renewal of the treatment may be necessary. Floyd says that his experience with the use of artificial pneumothorax has shown him that only a relatively small

number of cases are really suitable for this treatment. Well marked or advanced strictly unilateral cases are not common even in large clinics for pulmonary tuberculosis, and some observers believe that such cases are always bilateral. If this type of case is strictly adhered to the results obtained will be uniformly good and the percentage of patients markedly improved or arrested will be as large as 40 per cent. or 50 per cent. If, on the other hand, almost any otherwise hopeless case in which satisfactory compression can be obtained, is given a chance of obtaining relief at least from persistent symptoms, the results will not be brilliant. Artificial pneumothorax will be of real aid in the chronically recurring tuberculous pleural effusions, and in some cases of bronchiectasis and pulmonary abscess in which the inflammatory conditions are not too extensive. But even if this group of diseases may be benefited by the use of this method its field in the treatment of diseases of the chest will still be relatively a narrow one. It is most applicable where the patient is under the supervision of hospital or sanitarium management and has failed to do well with the older and well-established methods.

An Experimental Study of the Antiseptic Value in the Urine of the Internal Use of Hexamethylenamin.—HINMAN (*Jour. Amer. Med. Assoc.*, 1913, lxi, 1601) in his conclusions states that the conversion of hexamethylenamin into formaldehyde is a simple chemical process which will readily occur in an acid medium but will not occur in an alkaline medium. The amount of excretion of hexamethylenamin in the urine is influenced by the size of the dose, by the frequency of administration and by the character of the changes that occur in the acid contents of the stomach. The amount of the subsequent conversion of this hexamethylenamin in the urine is dependent on the degree of urinary acidity, on the duration of exposure to the influence of this acidity and on the percentage concentration of the drug in it; and in order to give formaldehyde conversion in antiseptic amounts the urinary acidity should be greater than 2 c.c. of tenth-normal sodium hydroxide for 10 c.c. of urine. A low acidity may be temporarily increased by feeding certain acid-producing drugs, and this increase in acidity may often be maintained by giving these drugs alternately. Disease of the kidney has no influence whatsoever on the formaldehyde content of the urine. At the level of the kidneys hexamethylenamin in doses of 15 grains three times a day has no antiseptic value. Formaldehyde is present in the bladder urine in some amount in practically every case receiving 15 grains of hexamethylenamin by mouth three times a day, but this dosage is too small a routine from which to expect a reasonable antiseptic benefit in every case. The allied hexamethylenamin compounds do not give greater antiseptic values than pure hexamethylenamin. Hexamethylenamin is dispensed under many proprietary names, such as urotropin, formin, aminoform, cystogen, etc. Certain of these are less irritant, but none of them liberate more formaldehyde than the pure drug, and in most cases not so much. In addition to these there are a number of other proprietary preparations for which an action superior to hexamethylenamin is claimed but of four of these, helmitol, hexal, saliformin and myrmalyde, studied by Hinman, none gave as good a formaldehyde content as hexamethylenamin.

Intravenous Injections of Neosalvarsan with Syringe.—ZUMBURCH (*Wien. klin. Woch.*, 1913, xxvi, 1305) has given 337 intravenous injections of neosalvarsan in concentrated form by means of a syringe to 149 cases and considers that this method is far preferable to the gravity method of injecting dilute solutions of neosalvarsan. The chief advantages are the rapidity of treatment and the simplicity of the apparatus. The usual dose of 0.75 to 0.9 gm. of neosalvarsan is dissolved in 20 c.c. of solution and the injection is made by means of a 20 c.c. Ricord syringe. The only apparatus required consists of the syringe, needle, and sterile glass for making the solution.

The Intravenous Injection of Neosalvarsan in Concentrated Solution.—SCHRIBER (*Münch. med. Woch.*, 1913, lx, 1993) advocates the use of intravenous injections of a concentrated solution of neosalvarsan in place of the injection of the more dilute solution, usually given. The usual dose of 0.75 gm. of neosalvarsan dissolved in 10 c.c. of normal salt solution is injected directly into the vein by their method. Schriber has used these injections extensively and has given them to individual patients once a week over long periods of time without untoward effects. These injections give rise to no greater general reaction than those observed when the drug is given in more dilute solutions. No irritation at the site of injection has been observed with the use of this concentrated solution. Schriber is of the opinion that this method of injection is a distinct advance and makes neosalvarsan a practical drug for general practice.

Radium in Internal Medicine.—ROWNTREE and BAETJER (*Jour. Amer. Med. Assoc.*, 1913, lxi, 1438) give a summary of the physiological and therapeutic effects of radium as observed by many European authors. They find that the consensus of opinion is that the use of radium is attended with an increased urinary uric acid output and that disappearance of deposits (tophi or artificial deposits) is hastened. Radium is given in the form of baths in radio-active water and the benefits derived in many of the European spas is now attributed to the inhalation of radium emanation as it constantly escapes from the surface of the water. Radium is also given by subcutaneous injection, as a local application such as compresses to the skin and internally by drinking radio-active water. The best method is by inhalation, but this is very expensive requiring a special air tight room or cabinet. The authors believe that the value of radium is unquestionably established in chronic and subacute arthritis of all kinds (luetic and tuberculous excepted), acute and chronic joint and muscular rheumatism, in gout, sciatica, neuralgia, polyneuritis, lumbago, and the lancinating pain of tabes. In certain other diseases it is said to be of value, but here the evidence is not so convincing. This list is a varied one and includes chronic bronchitis, chronic pharyngitis, pneumonia, myocarditis, arteriosclerosis, vasomotor disturbances, Raynaud's disease, scleroderma, idiopathic enlargement of the lymph nodes and chronic constipation. Rowntree and Baetjer give tables to show the results obtained in the different diseases of 471 cases of chronic arthritis and chronic rheumatism as described by 23 authors. 371 were improved, and of these 102 were cured. Of 24 cases of arthritis deformans reported

by seven observers, 16 showed improvement. Of 59 cases of muscular rheumatism, 49 were either cured or improved. Of 166 cases of gout, 86 were influenced for the better. Of 59 cases of neuralgia, 47 were improved, of which 25 were practically cured. Of 115 cases of sciatica treated by 18 different authors, benefit was observed in 91 instances, although some of the cases were of long standing. In 44 cases of tabes, the lightning pains were alleviated in 26 instances, for long periods of time in some instances. Rowntree and Baetjer also cite a series of 18 cases including a considerable variety of affections where their personal experiences with this method of treatment were not so favorable, as the published work of European observers indicates. However, they do not wish to draw conclusions from so small a series and furthermore the cases treated have been a severe test of the treatment since they comprised these cases which had been given the benefit of all other forms of treatment without bony improvement. Rowntree and Baetjer believe that the introduction of radium emanatoriums in a large number of German spas, as well as the establishment of a radium institute in Berlin express confidence in this method on the part of the profession abroad and this subject should be carefully investigated until its real value can be definitely established and its limitations rationally outlined.

PEDIATRICS

UNDER THE CHARGE OF

LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.,

OF PHILADELPHIA.

Treatment of Diphtheria Carriers with Bouillon Cultures of Staphylococcus Pyogenes Aureus.—J. D. ROLLESTON (*Brit. Jour. Child. Dis.*, 1913, x, 298) reviewed the reported cases of diphtheria carriers treated by cultures of the staphylococcus pyogenes aureus and found the total number reported to be about 50, and with a few exceptions the observations were confined to the United States. In almost all the cases, the throats of the carriers were sprayed or swabbed with a bouillon culture of the staphylococcus. In most of the cases negative cultures were obtained in 48 to 72 hours after this form of treatment had been begun. The method was shown to be most successful in typical carrier cases and less so in cases with clinical symptoms. Rolleston used this treatment in 10 cases, comprising 4 adults, and six children. In 8 the fauces and in 2 the nose alone had been involved and all had reached an advanced stage of convalescence. The palate, fauces, and in the nasal cases the nostrils as well were sprayed 3 or 4 times a day with broth cultures of pure staphylococci incubated for 18 to 24 hours. In all but 2 cases a mild form of sore throat was produced with considerable malaise but with very slight fever. These symptoms were of short duration and were not followed by any complication. The average time the treatment was begun in this series was the fifty-second day of the condition. In the 6 faucial cases the findings became

negative within two to seven days after starting treatment. In the 2 nasal cases it was ineffective. This method should not be employed except in the late stage of convalescence and it is best to confine it to chronic carriers. It offers the best form of treatment but entails some degree of discomfort. Among the previous investigators no complications were noted except Lorenz and Ravenel who mention coryza, very mild laryngitis, and nasal furuncles occurring among their cases.

Acute Acid Intoxication in Children.—THOMAS C. MCLEAVE (*Jour. Amer. Med. Assoc.*, 1913, lxi, 1764) reviews the theories of production of acid intoxication and gives the symptoms and treatment. This condition may occur in children aged from eight months to ten years. It may usher in an acute infectious disease or the attacks may be recurrent. Some chronic focus of infection is probably always present, such as an inflamed appendix or more commonly diseased tonsils or adenoids. The toxins from whatever source cause a condition in the liver function which produces faulty metabolism of carbohydrates and especialty of fats and proteins. As a result, toxic bodies such as acetone and diacetic acid appear in large quantities in the urine and acetone is markedly noticeable on the breath. The nervous element is undoubtedly a factor in producing the condition, and a catarrhal condition of the nasopharynx is usually present. Characteristic symptoms are anorexia, coated tongue, a bluish pallid ring around the mouth and eyes with flushing of the cheeks, coryza with variable cough, pallor, sunken eyes, dry and cracked lips, foul breath with odor of acetone, vomiting of large amounts of fluid, rapid emaciation, scanty urine, constipation, and moderate fever. The duration of the attack is from two to seven days but deaths from this cause are very rare. The treatment consists of eliminating any possible focus of infection, a dietary low in fats with ample amounts of carbohydrate. Citrus, fruit juices, and grape-juices are also valuable. Fatigue and undue excitement should be avoided. Sodium bicarbonate in one to two dram doses weekly, and periodic emptying of the large bowel tend to abort the attacks. During the attack sodium bicarbonate can be given in 60-grain doses every three or four hours by mouth or rectum. Sugar must be given, preferably dextrose, in 4 per cent. solution with alkali, either by mouth or rectum. Both the sodium bicarbonate and the dextrose can be given in solution intravenously if the case is urgent. Saline infusions are given for the drying-out of the tissues, and opium, chloral, and the bromides control the nervous manifestations.

Some Unusual Phases of Child Hygiene.—MARY SUTTON MACY (*Archiv f. Pediatrics*, 1913, xxx, 848) points out the importance of protecting the child (from infancy to adolescence) from the ill effects of psychic trauma, which are not by any means all sexual. The epidemic of Freudism in this country threatens to restrict the term "psychic trauma" in its meaning to the sexual character. Macy mentions a large number of cases in children from ten to eighteen years initiated by a psychic trauma, which closely simulated a beginning Basedow's disease. In none of these cases has the initial shock been in any way sexual. She also mentions 30 cases of chorea having a history of psychic trauma, in no way sexual, as the point of origin

for the neurotic symptoms. She calls attention to contributory effects of nervous shock in initiating both of these nervous conditions. She defines psychic trauma as a term embracing all nervous shocks which arrest or retard mental processes, and includes under the term acute shock from fright, anger, grief, joy, fear, etc., and chronic shock from repeated disappointment and mental fatigue from uncorrected defects of vision, hearing, etc. In public schools a crowded curriculum and forcing children forward at a fast rate is a detriment to health and tends to produce mental and physical inadequacy. Both diseases mentioned above are aggravated, if not more or less indirectly caused by psychic trauma. Therefore, all obvious causes of nervous strain within control of public school authorities should be prevented. The majority of those in immediate charge of our schools are absolutely unintelligent on this vital subject of caring for the health of the child. Medical school inspection has done practically nothing to control and prevent disability from over-pressure, crowded curriculum, and nervous strain during puberty and early adolescence.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Imidazolylathylamin in Obstetric Practice.—JAEGER (*Zentralbl. f. Gynäk.*, 1913, viii) reports the results of this agent in obstetric practice. It is a preparation derived from ergot and from histidin by the action of nitric acid. It is supposed to stimulate unstriped muscular fibers. It acts upon the muscular fibers of the uterus, the muscular tissue in the bronchial tubes, the iris, and the bladder. It probably has some action upon the unstriped muscle of the bowel, the arterioles, and the spleen. It does not seem to affect the heart directly. On blood pressure, it produces a differing action in different animals. In some, the blood pressure rises; and, in others, sinks. The action of the salivary glands and pancreas is increased by the hypodermic injection of this substance, while the secretion of urine is not influenced. This agent was tried in the case of a puerperal woman, in doses of 30 drops of a solution 1 to 1000, given three times daily. This agreed with the patient, and produced no disagreeable effects. It was compared with other preparations of ergot. Involution seemed to proceed more efficiently, and the after-pains were less frequent, and shorter. It was used to increase the vigor of uterine contractions in 25 cases, 13 primiparæ and 12 multiparæ. It was given by intramuscular injection in the gluteal region, or subcutaneously in the arm or upper portion of the thigh. These injections were not painful, but produced redness at the point where the needle entered. Varying doses were

tried, and the effect noticed upon the mother and the child as well. No influence could be detected upon the fetus, but in some of the mothers the head and face were flushed, the heart acted more vigorously, there was erythema, flatulence, and vomiting. In the experience of Jaeger, small doses produced the best results, and on the whole, the remedy seemed quite as efficient, and in many respects better than the usually employed preparations of ergot.

The Complications and Variations of Eclampsia.—Halliday Croom (*British Med. Jour.*, December 21, 1912) calls attention to what he terms *pseudo-eclampsia*. His patient was a woman seven months, in her second pregnancy, who had severe fits for two days, with marked coma. The urine was normal; there was no evidence in the eyes or limbs of any lesions of the nervous system. The patient died, and at autopsy a cholesteatoma the size of an orange was found in the brain near the anterior end of the left cerebral hemisphere opposite the superior middle and inferior frontal convolutions. In another case in which eclampsia was suspected, at autopsy meningitis was found to be the cause of the convulsions. In discussion, Fordyce described two cases treated as eclampsia in which at autopsy cerebral hemorrhage was found. The etiology of eclampsia was the subject of discussion in a joint meeting of the sections of Pathology and Obstetrics of the British Medical Association, (*British Med. Jour.*, October 26, 1912). Ballantyne believed that eclampsia was the result of pregnancy with renal and hepatic inadequacy, and possibly external and internal disturbances, which increased the strain upon the kidneys and nervous system. Unquestionably, toxemia causes eclampsia. Primary toxemia may result from disturbances in the mutual metabolism of mother and fetus, while the secondary toxemia which develops and causes the convulsions must be left to changes in the kidneys, liver, and other glands. The successful treatment addressed to toxemia supports its claim to be the cause of eclampsia. In his personal experience, his results improved greatly in proportion as he treated eclampsia for the toxemic condition present, his maternal mortality under this treatment being 9.6 per cent. Teacher reviews the literature of the subject, and describes the changes found in the kidneys and suprarenals in 21 cases. Smyly reviews the literature of the subject, and considers that Stroganoff's statistics indicate successful treatment. Kerr used medicinal treatment in cases where the cervix was obliterated and there were indications that labor was about to take place. If the birth canal is undilated, he would deliver by section.

Heinrichsdorff (*Zentralbl. f. Gynäk.*, 1912, iv) reports the case of a primipara who died half an hour after delivery with forceps, after moderate hemorrhage, and apparently from failure in the action of the heart. At autopsy, the liver was found enlarged, with extravasations of blood under the capsule and staining in various portions of the gland. The interesting feature of the case was the absence of convulsions, there being present hemorrhage and extensive lesions in the liver characteristic of eclampsia.

Ladinski (*Amer. Jour. Obstet.*, July, 1912) reports eclampsia complicated by the birth of a monster, consisting of two fetal bodies joined together through the trunk and with one head.

BAUREISEN (*Zeitschr. f. Geburts. u. Gynäk.*, 1912, Band lxxi, Heft ½) raises the question whether eclampsia is a reaction of immunity. He believes that placental tissue exercises the function of an antigen, and that disturbances of the nervous system in the first months of pregnancy, and in the digestive organs, are the results of the development of immunity through the absorption of placental products.

DIENST (*Archiv f. Gynäk.*, 1912, Band xcvi, Heft 1) has made experiments to determine the influence of fibrin ferments in the causation of eclampsia. He believes that pregnancy predisposes to derangements of the circulation, and that fibrin ferment is readily produced in excess. This may become a toxic product, and readily bring about degenerative changes seen in those organs most closely concerned in the process of metabolism.

Hematomyelia complicating eclampsia is reported by LEBICH (*Zentralbl. f. Gynäk.*, 1912, xxxivii). The patient was a primipara at term, in labor, and having severe eclamptic convulsions. Between the first and second the temperature rose to between 105° to 106° F.; the pulse was small and feeble. The patient complained of intense pain in the neck and right shoulder. The cervix was partly dilated and the head in the pelvic cavity. Delivery was effected by incising the cervix and using forceps. The child was living. After delivery, the blood pressure was 108, and the urine contained 12 per cent. albumin. There were no more convulsions, and the patient gradually recovered. She developed nervous symptoms of paralysis in some of the muscles, spastic in nature, and her final recovery was complicated by paresis in several groups of muscles.

Pseudo-eclampsia is the subject of a paper by POLANO (*Zeitschr. f. Geburts. u. Gynäk.*, 1912, Band lxx, Heft 2). He reports 2 fatal cases, with autopsy, one of whom had epileptic convulsions with albumin in the urine, and was delivered by incising the cervix and applying forceps. On autopsy there were extensive degenerative changes in the glandular organs and beginning hypostatic pneumonia. The second case was brought to hospital unconscious, the urine showing casts and albumin. The cervix was tightly closed, and the urine brownish-red in color. The patient was delivered by section, and, upon autopsy the characteristic changes in eclampsia were found in the various organs.

PERSSON (*Archiv f. Gynäk.*, 1912, Band xcviii, Heft 1) draws attention to the relation between eclampsia and puerperal paresis. While they are distinct conditions, their common element is the presence of fetal material in the blood of the mother. He believes that this material produces the characteristic alterations in the blood, and thinks he has had good results from the administration of potassium idoide. He believes that it produces this effect because it lessens the amount of saline material in the blood.

ESCH (*Archiv f. Gynäk.*, 1912, Band xcviii, Heft 1) takes up the familiar question of the toxicity of the urine in eclampsia. He believes in pregnancy that the toxicity of the urine is not much increased, while it is lessened during labor, increasing somewhat the fourth and fifth day of the puerperal period. From experiments upon animals he found that intracranial injections of urine from healthy, non-pregnant patients, from those with carcinoma of the uterus, from

those in labor and in the puerperal period, and from women having eclampsia, produces in guinea-pigs light or severe anaphylactic shocks; and this was confirmed by autopsy. Subcutaneous or intraperitoneal injections of urine from patients not evidently toxemic, produced no symptoms in white mice. Where decomposed urine, or altered urine was employed, death followed with hyperemia of the abdominal organs. The toxicity of urine measured by the temperature reaction was very little increased in healthy pregnant patients. In patients in labor, it was somewhat lessened, and in puerperal patients, somewhat increased. In 2 cases of severe eclampsia occurring during labor, the urine taken in the period of dilatation was exceedingly toxic, while in the third case there were slight convulsions, and the urine was scarcely altered from the normal.

A curious contribution to the therapeutics of eclampsia is made by WALCHER, JR. (*Zentralbl. f. Gynäk.*, 1912, xlii). Acting upon Sellheim's suggestion that the breasts contain toxins which have a part in the production of eclampsia, he has treated, in the clinic at Stuttgart, 11 cases of eclampsia by extracting colostrum from the breasts in many cases, followed by the infiltration of salt solution. The results seem to indicate that this procedure may be useful in checking convulsions.

ZINSSER (*Zeitschr. f. Geburts. u. Gynäk.*, 1912, Band lxx, Heft 1) has investigated the function of the kidneys in eclampsia. He believes that in eclampsia the chlorides are retained and not excreted normally by the kidneys, and that this has to do with the production of eclampsia. He has made observations to determine the percentage of sodium chloride in the blood of eclamptics, and also in the excretion of eclamptics at the time of the convulsions. His cases numbered 31, and for 14 he gives curves illustrating his observations. He finds that in eclamptic cases with dropsy, where there is a sudden and permanent arrest in the excretion of chlorides, usually in the form of chloride of sodium, and where there is no other clinical reason for this phenomenon, that this constitutes a symptom of dangerous and often fatal intoxication. When, on the other hand, the percentage of chlorides in the urine is high, it is a symptom which justifies a favorable prognosis.

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Prophylaxis of Carcinoma of the Cervix.—BOSSI (*Zentralbl. f. Gyn.*, 1913, xxxvii, 1000) has recently issued an appeal to all gynecologists to consider more carefully what he considers the true prophylaxis of cervical cancer, namely, the early, *surgical* treatment of all minor, non-malignant injuries and inflammations of the cervix. To treat

such conditions with local applications, caustics, etc., as is so commonly practiced, is, in his opinion, utterly unjustifiable; the chronic inflammations and tissue hyperplasias that are caused by such treatment are, he thinks, often the direct cause of a subsequent malignant development. All ulcers of the cervix should be removed, hyperplastic areas of endometrium curetted away, and small lacerations repaired by suitable plastic operations; if this policy were uniformly carried out we would see vastly less uterine cancer than is now the case. Bossi says that as he looks back on his years of practice he finds that he has performed such plastic operations on over 7000 patients, and so far as he has been able to determine, in no single instance has one of these women subsequently developed a cervical carcinoma. A record such as this, together with the fact that cancer is in no wise contagious, is for him proof positive that the disease is absolutely non-microbic, but purely histologic in origin; he thinks that a truly humanitarian and scientific undertaking would be a propaganda against uterine cancer which should have for its basis the early, reparative, surgical treatment of benign affections of the cervix and uterine cavity.

Hydrotherapy in Gynecology.—In a communication presented before the Congress of Physicians and Naturalists, held in Vienna last September, KLEIN (*Frauenärzt*, 1913, xxviii, 541) reports on the results obtained in the treatment of various gynecological conditions by means of hydrotherapy in the year and a half since the plant was installed in the Wertheim Clinic. He says that the results were in general exceedingly good, and in some instances most astonishing. The indications for this form of therapy include both functional and organic disturbances; especially good results were obtained in the treatment of all the types of disease commonly grouped under the term "sexual neurasthenia," but many true organic conditions also show marked improvement or complete cure. Among these may be mentioned particularly perimetric adhesions, exudates following salpingo-oöphorectomy, extensive parametric exudates, chronic inflammatory adnexal masses, etc. In conjunction with various forms of hydrotherapy, mud baths have also been found of great benefit in some of these chronic inflammatory lesions. Klein emphasizes the importance of a thorough mastery of the technique of this form of therapy in all its details, and thinks that much of the skepticism which exists toward it is the result of poor results obtained from a lack of knowledge as to the indications and contra-indications on the one hand, and of the technique on the other.

Formalin Treatment of Leukorrhea.—The technique and results of a new form of treatment for leukorrhea, recently introduced at the Baudeloque Clinic, are described by LE MASSON and MARCHAL (*Ann. de Gyn. et d'Obst.*, 1913, xl, 731). This consists in the introduction into the vagina of nascent formalin gas, a process which may be accomplished by one of several methods. The simplest is merely to fold a few crystals of potassium permanganate in a small square of gauze, sprinkle it well with full strength formalin solution, and introduce it by means of dressing forceps into the vagina through a speculum.

More thorough and satisfactory application may be secured, however, by the use of some form of vaporizing apparatus, while for use by the patient herself, a special appliance, known as the "formojecteur" has been devised. This consists of an egg-shaped receptacle, which may be taken apart in the middle, and which contains a separate compartment for water, the whole being connected with a short tube and douche nozzle. To use it, the egg-like receptacle is opened, and 1 gm. of crystalized potassium permanganate placed in the bottom. It is then closed again, and the water compartment filled with 1 c.c. of a mixture of equal parts of commercial formalin and water. The patient then introduces the douche nozzle into the vagina in the ordinary manner, and by pressing with her thumb on a small piston which communicates with the chamber containing the formalin solution, forces this into the main receptacle containing the permanganate, with the resulting generation of formalin gas. This, of course, passes off through the nozzle into the vagina. Le Masson and Marchal have found formalin gas, applied in this way, to have a marked drying action on leukorrheal discharges, transforming profuse mucopurulent discharges into a thin, watery type, which in turn soon completely disappears. This dessicating action is followed by a certain amount of tissue retraction, resulting in cicatrization of mild degrees of cervical endometritis, and diminution of erosions about the external os. To be thoroughly efficacious, however, the treatment should be kept up faithfully for at least six weeks or two months, the home applications with the formojecteur being supplemented from time to time by more thorough treatments by the physician. Chemical tests have shown the formalin vapors to be absolutely neutral, so that no deleterious consequences, such as the production of sterility, are to be feared. The treatment is entirely painless, and appears to deserve a place in the realm of medical gynecology.

Formation of an Artificial Ureter.—The results of some interesting attempts to form artificially a segment of ureter from the abdominal wall are reported by STRAUSS (*Surg., Gyn., and Obst.*, 1914, xviii, 78). The work was performed on dogs, and while purely experimental as yet, may well prove to be of practical application to clinical surgery. The technique was, very briefly, to form a pedunculated flap from the transversalis muscle, fascia, and peritoneum, the peritoneum and abdominal wall being then closed, so as to make the remainder of the operation wholly extraperitoneal. The ureter was then exposed, and two or three inches of it resected; the two cut ends were then anastomosed into the upper and lower end of the flap respectively, this latter being rolled up like a sleeve, with the peritoneal surface inside, and closed with a continuous suture of fine arterial silk, which material was also used for the anastomoses. The operation was performed on four dogs, all of which survived until killed at intervals of from five and a half to seven months after operation. The findings in the artificial segment of ureter were extremely interesting: In three of the animals it had apparently functionated well, though in one a calculus was found lodged in the distal anastomosis, having the end of a silk thread for a nucleus. In the other 2 cases which functionated well no obstruction was found, but in one the artificial ureter was dilated

to form a pouch, and was associated with slight hydronephrosis. In the fourth dog a contraction was found, forming an almost complete obstruction at the lower anastomosis, with corresponding dilatation of the ureter and hydronephrosis. In every case the artificial portion of the ureter was transformed into a rigid, non-collapsible tube, which showed histologically in place of the peritoneum a typical transitional epithelium, such as is found in the normal ureter, surrounded by a thin layer of areolar tissue; outside of this, replacing the transversalis fascia, a definite layer of well organized bone had formed, with typical osteoblasts, and blood and lymph vessels. The transversalis muscle, forming the outermost coat, showed no change. Strauss thinks that the epithelium probably resulted from a proliferation of the epithelium of the ureter, the basement membrane of the peritoneum acting as a matrix for its implantation. The bone formation is to be explained, he thinks, by slight degenerative changes caused in the tissue by the irritating action of the urine, followed by partial calcification of this tissue from lime salts brought to it in the body fluids, together with the osteogenetic potentiality inherent in the particular group of muscles and fascia used for the flap. Strauss reports that he is continuing his experiments with free, non-pedunculated flaps, and has three dogs now alive three months after such operations.

Tuberculous Origin of Ovarian Cysts.—POLLOSSON and VIOLET (*Lyon Chirurgical*, 1913, x, 340) advances the theory that many of the so-called simple or serous cysts of the ovary are in reality of inflammatory origin, by far the most important type of inflammation in this connection being tuberculosis. They have observed that not infrefrequently ovarian cysts, showing themselves absolutely nothing characteristic of tuberculosis, occur in conjunction with tuberculous tubal or peritoneal lesions; they report, for instance, a case in which a cyst the size of an adult head, containing two liters of serosanguineous fluid, was attached to a tube showing distinct tuberculous changes, but without suppuration. Histologically, the cyst appeared to be of corpus luteum origin. In two other instances, tubal tuberculosis (producing no symptoms, but demonstrated histologically) was present, associated with bilateral ovarian cysts the size of oranges or larger. Pollosson and Violet believe that in such cases there is a distinct etiological relationship between the tubal lesion and the cyst formation, since the latter occurs only in conjunction with attenuated or slowly developing forms of tubal tuberculosis; in acute conditions the ovary apparently does not undergo the cystic change. In a second group of cases the cystic ovaries are associated with healed tubal or peritoneal tuberculosis. In the walls of the tubes of such patients there are often found small nodules containing caseous matter, occasionally the continuity of the tube may be completely interrupted, and all the pelvic organs buried in adhesions. In a case of this type operated on by Pollosson, the clinical history revealed the fact that at the age of four years the patient had had a severe attack of what had been diagnosed at that time as tuberculous peritonitis. At operation the characteristic conditions described above were found, and the ovaries were cystic. A third group comprises patients with cystic ovaries, without characteristic lesions of the surrounding organs,

but whose family history is such as to lead to a strong suspicion of a tuberculous condition. In many of these, although nothing typical is found at operation, this suspicion is subsequently confirmed by the development of tuberculosis somewhere else in the body. Polloson and Violet believe that the tuberculous inflammation acts by causing ovarian congestion, hyper-maturation of follicles, and excessive formation of atretic follicles, these conditions leading to the formation of sclerocystic ovaries, hematomas, and large simple cysts. They do not, however, believe that tuberculosis plays an etiological role in the production of true pseudomucinous or papillary cystomas.

DERMATOLOGY

UNDER THE CHARGE OF

MILTON B. HARTZELL, M.D.,

PROFESSOR OF DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

The Treatment of Lupus Vulgaris with Hot Air.—RAVAUT (*Bull. de la Société Francaise de Dermatologie et de Syphiligraphie*, 1913, No. 2), at a seance of the French Society of Dermatology and Syphilis, presented a case of nodular, non-ulcerating lupus of the jaw and ear which he had treated with great success with hot air combined with curettement. Under chloroform anesthesia the affected area was vigorously scraped with the curette and afterward cauterized with hot air at a temperature of 700° C. The eschar was detached at the end of ten days, and a month later cicatrization was complete, the scar being supple and non-retractile. About four months later a small suspicious point beneath the ear was cauterized with the hot air again. Two years later there had been no recurrence. Properly employed Ravaut thinks this the method of choice in the treatment of lupus; he knows of no other method which cures as quickly.

The Course the Virus of Herpes Zoster Takes to Reach the Nerve Ganglion.—MONTGOMERY (*Jour. Cutaneous Diseases*, March, 1913) believes that herpes zoster is an infection, and that the virus enters the lymphatics of the nerve sheath and travels from the periphery to the nearest ganglion. He thinks this theory best explains the neuralgia which often precedes the eruption; the unilateral distribution of the disease, its most frequent occurrence on the head, neck, and upper part of the trunk, the much more frequent involvement of the sensory than the motor nerves, the limitation of the eruption to one or two nerves, the partial inflammation of the Gasserian ganglion, the frequent great severity of ophthalmic zoster, and the enlargement of the lymphatic nodules along with the eruption.

Chronic Raynaud's Symptoms, Probably on a Syphilitic Basis, Associated with Livedo Reticulata.—WEBER (*British Jour. Dermat.*, March, 1913) reports the case of a married woman, aged fifty-four years, who had suffered from the symptoms of Raynaud's disease for

fourteen years, chiefly in the left foot and hand, slight gangrene of the toes of the left foot having occurred on one or two occasions. She had had retinal hemorrhages in the left eye and suffered from recurrent attacks of temporary amblyopia. All over the patient's back and most noticeably over the extensor surface of the extremities was an unusually well-marked, net-like, livid mottling of the skin. In Weber's opinion, both the Raynaud's symptoms and the livedo were probably "on a syphilitic basis," although the Wassermann reaction was negative; he also though that the mitral stenosis from which the patient suffered favored the production of the symptoms.

The Etiology of Alopecia Areata.—SABOURRAUD (*Annales de Dermatologie et de Syphiligraphie*, No. 2, 1913) has observed, especially in women, a more or less close relationship between diseases of the genital apparatus and alopecia areata. He finds that there is a variety of alopecia which follows the menopause and even prolonged suppression of the menses. It may occur after ovariotomy, and, more rarely, in the course of pregnancy and even in the course of several successive pregnancies; this form seems to be relatively benign. In one case an alopecia supervened in a man coincidently with a double tuberculous orchitis, and it became total and permanent before a double castration was performed. Sabourraud (*Ibid.*, No. 3, 1913) has likewise observed certain chronic and grave forms of alopecia areata which seemed to be directly connected with exophthalmic goitre, growing better and worse parallel with the course of the goitre.

Hemorrhagic Erythema Multiforme with Fatal Termination.—DE AMICIS (*Archiv f. Dermatologie u. Syphilis*, Band cxvi, Heft 2) reports with considerable clinical and histological details the following unusual case of erythema multiforme: A coachman, aged twenty-five years, alcoholic and syphilitic, after long exposure to cold and rain, was seized with pain and swelling of the joints accompanied by sore throat and high fever. The face was markedly swollen, so that it was impossible to open the eyes and there was a macular eruption which became confluent, upon the face and upper extremities. Upon his admission to the hospital the patient was extremely prostrated, and the entire skin was covered with a papular eruption, most abundant upon the face and upper extremities, in part discrete, in part confluent, forming gyrate and polycyclic patches. The mucous membranes of the lips and mouth were likewise involved; they were swollen and cyanotic with hemorrhagic spots and erosions, and on the uvula and the left palatal half-arch there was an extensive necrotic lesion covered with a croupous exudate. The urine contained a small quantity of albumin. The patient complained much of abdominal pain with vomiting after his admission to the hospital, the prostration increased and death occurred two weeks later. As the result of the clinical study and the findings at the autopsy, De Amicis concludes that the case was one of idiopathic polymorphous erythema of the Hebra type, and that its severity was due in part to individual predisposition and in part to the lowering of the patient's powers of resistance by alcoholism and syphilis.

Mesothorium in Dermatology.—KUZNITZKY (*Archiv f. Dermatologie u. Syphilis*, Band cxvi, Heft 2) reports his experience with mesothorium in the treatment of various diseases of the skin, such as, carcinoma of the skin, vascular and pigmented nevi, lupus vulgaris, lupus erythematosus, etc. Round capsules of 5, 10, and 15 mm. diameter, containing 5, 10, 16 and 20 mg. of mesothorium were bound upon the part to be treated with adhesive plaster, in such a manner as to prevent shifting, and allowed to remain from forty minutes to two hours, the time depending upon the amount of mesothorium contained in the capsule and the depth of the disease. In 24 cases of carcinoma 19 were clinically cured, 2 were greatly improved, and in only one was the treatment a complete failure. In 13 cases of angioma there were no failures, and the cosmetic effect was excellent. In the treatment of nævus flammeus (portwine stain) mesothorium is to be preferred to the *x*-rays, radium, and carbon dioxide on account of the simplicity of its application and the certainty of its effect. In lupus vulgaris no cures were obtained, although improvement was noted. In lupus erythematosus the results of treatment in 8 cases were extraordinarily favorable.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT; SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL.

Action of Lymph Gland Juices on Tubercle Bacilli.—MARFAN, WEILL-HALLE and LE MAIRE (*Jour. de Physiol. et de Path. gén.*, July 15, 1913, xv, No. 4) determined that the tissue of lymph nodes and of the spleen exercises an attenuating action *in vitro* upon tubercle bacilli, the liver definitely, but less so. The serum appears to exercise no attenuating effect, and the brain pulp actually an exalting effect. Marfan, Weill-Halle, and Le Maire can only offer hypothesis by way of explanation, and admit that the result may be due to the products of autolysis, and that thus the same process will not be at work *in viro*. However, certain results have shown a parallel process in the living animal.

Changes in the Circulatory System in Acute Edema of the Lungs.—KOTOWSCHTSCHIKOW (*Zeitsch. f. exper. Path. u. Ther.*, 1913, xiii, Heft 3, 400) has undertaken a very complete series of experiments dealing with various problems relating to the power of the heart, and changes in the arterial system during and after the production of acute edema of the lungs. The most frequently observed form of general acute edema of the lungs is toxic; less often lesions of the bloodvessel walls produce an edema of a mechanical nature, while

edema of a purely neural origin is yet unobserved. Anything which prevents the flow of blood out of the lesser circulation into the left auricle may readily produce a general acute mechanical edema of the lungs, as well as anything which rapidly lessens the calibre of the lung capillaries. In such a case the pressure in the pulmonary arteries is greatly increased, as is also the work of the right ventricle, while the general arterial system, that is, the greater circulation, is apt to indicate a fall of pressure. In the human being an acute edema of the lungs may be brought about by damage to the flow of blood into the left auricle, rapidly produced by, for example, a tumor, an aneurysm, even a thrombotic formation in the vessel itself. Experimental toxic edema is readily produced by different poisons, but while it is generally accompanied by a heightened pressure in the pulmonary artery, and so increased contraction in the right ventricle, nevertheless it may exist even in the absence of these phenomena. The mechanical production of such an edema seems to depend upon an increase in the size of the pores of the lung capillaries, which the active movement of the blood increases, of which an increase of pressure in the pulmonary arteries is the forerunner. The edema which occurs in many cases after the inhalation of ether is apparently of this nature. A lowering of pressure occurs equally in the mechanical and toxic edema, while heightening of pressure, or a normal pressure on the other hand, occurs only in toxic forms. The pulse exhibits nothing characteristic; the beat may be slow or rapid, regular or arrhythmic. In mechanical edema the pulse may reflect a descent of the arterial pressure, and in any case the character of the pulse will have considerable meaning as indicating the state of the heart itself with reference to overcoming the edema. Kotowschtschikow states that the so-called neuropathic edema as a primary occurrence experimentally produced has not yet been observed, and considers that the number of clinical observations in favor of its occurrence are not yet sufficiently numerous to allow a definite opinion upon it.

Notice to Contributors.—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this* JOURNAL.

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *provided the request for them be written on the manuscript.*

All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1927 Chestnut St., Phila., Pa., U. S. A.

CONTENTS

ORIGINAL ARTICLES

Cholecystitis without Stones or Jaundice in its Relation to Chronic Pancreatitis 469
By WILLIAM J. MAYO, M.D., Rochester, Minnesota.

The Treatment of Pylorospasm in Infancy 474
By JOHN RUHRÄH, M.D., Professor of Diseases of Children in the College of Physicians and Surgeons, Baltimore, Maryland.

Tuberculosis of the Spleen, Septic Infarction, Polycythemia, Splenectomy 479
By JOHN DOUGLAS, M.D., Surgeon to Bellevue Hospital; Assistant Surgeon to St. Luke's and General Memorial Hospitals, and A. B. EISENBREY, M.D., Assistant Surgeon St. Luke's Hospital, New York.

Giant Tumors of the Conus and Cauda Equina 493
By JOSEPH COLLINS, M.D., Physician to the New York Neurological Institute, and CHARLES A. ELSBERG, M.D., Surgeon to the New York Neurological Institute, New York.

Some Cases of Hypotension Associated with a Definite Symptomatology 503
By EDWARD H. GOODMAN, M.D., Associate in Medicine in the University of Pennsylvania; Assistant Physician to the University and Philadelphia General Hospitals; Consultant to the University Hospital Medical Dispensary, Philadelphia.

The Clinical Significance of Diastolic and Pulse Pressure 514
By PERCIVAL NICHOLSON, M.D., Assistant Physician in the Dispensary of the Children's Hospital, Philadelphia.

The Inhibitory Action of Certain Anilin Dyes upon Bacterial Development (Second Communication) 524
By CHARLES E. SIMON, B.A., M.D., Professor of Clinical Pathology and Experimental Medicine at the College of Physicians and Surgeons, Baltimore, Maryland. Assisted by MARTHA A. WOOD, M.D., of Houston, Texas.

Diagnostic Value of Percutaneous Tuberculin Test (Moro) 540
By EDWARD B. KRUMBHAAR, M.D., Fellow in Research Medicine, University of Pennsylvania; Physician to the Medical Dispensary, Pennsylvania Hospital; and JOHN H. MUSSER, JR., M.D., Physician to the Philadelphia General Hospital; Physician to the Dispensary of the Presbyterian Hospital; Instructor in Medicine, University of Pennsylvania, Philadelphia.

The Successful Removal of a Tumor from the Frontal Region of the Brain 550
By THEODORE DILLER, M.D., Visiting Physician to St. Francis' Hospital, and ROBERT T. MILLER, JR., M.D., Surgeon to St. Francis' Hospital, Pittsburgh.

The Total Non-protein Nitrogen of the Blood in Pregnancy and Eclampsia 556
By Clifford B. Farr, A.M., M.D., and Philip F. Williams, M.D., Philadelphia.

Prolapse of the Ovary: Its Rational Management 561
By Chauncey D. Palmer, M.D., Emeritus Professor of Obstetrics and Gynecology in the Medical Department of Cincinnati University.

Precocious Development of the External Genitals Due to Hypernephroma of the Adrenal Cortex 568
By Henry D. Jump, M.D., Henry Beates, Jr., M.D., and W. Wayne Babcock, M.D., Philadelphia.

Symptoms Suggesting Pituitary Disorder 575
By Earl D. Bond, M.D., Clinical Director and Pathologist in Danvers State Hospital, Hathorn, Massachusetts.

The Value of Auto-inoculation in Pulmonary Tuberculosis 579
By Harry Lee Barnes, M.D., Superintendent of State Sanatorium, Wallum Lake, Rhode Island.

The Early Symptomatology of Cancer of the Esophagus 583
By Henry H. Janeway, M.D., Assistant Surgeon to the City Hospital, New York.

REVIEWS

Anatomy and Physiology. A Text-book for Nurses. By John F. Little, M.D. 589
Blood Pressure from the Clinical Standpoint. By Francis Ashley Faught, M.D. 589
Hygiene of Sanitation. A Text-book for Nurses. By George M. Price, M.D. 591
The Practitioner's Encyclopedia of Medicine and Surgery in all their Branches. By J. Keogh Murphy, M.C. (Cantab.), F.R.C.S. . . 591
What Heart Patients Should Know and Do. By James Henry Honan, M.D. 592
The Elements of Bacteriological Technic; a Laboratory Guide for Medical, Dental, and Technical Students. By J. W. H. Eyre, M.D., M.S., F.R.S. (Edin.) 593
A Manual of Surgery. For Students and Physicians. By Francis T. Stewart, M.D. 594
Practical Bacteriology, Microbiology, and Serum Therapy (Medical and Veterinary). A Text-book for Laboratory Use. By Dr. A. Besson. Translated and adapted from the fifth French edition by H. J. Hutchens, D.S.O., M.A., M.R.C.S., L.R.C.P., D.P.H. (Oxon.) 594
Dorland's American Illustrated Medical Dictionary. Edited by W. A. Newman Dorland, A.M., M.D. 595
Handbook of Physiology. By W. D. Halliburton, M.D., LL.D., F.R.C.P., F.R.S. 596

Surgical Experience in South Africa, 1899–1900. By G. H. Makins, C.B., F.R., C.S. 597
Skin Diseases in General Practice. By Haldin Davis, M.D. 597
Aids to Gynecology. By S. Jervois Aarons, M.D., (Edin.), M.R.C.P., (Lond.) 598
The Tonsils and the Voice. By Richard B. Faulkner, M.D. 598

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D., AND ROGER S. MORRIS, M.D.

Cultivation of the Organism of Epidemic Poliomyelitis 599
The Production of Acetone Bodies in the Living Animal. 600
The Fatiguability of the Kidneys 600
The Secretion of Urotropin by the Mucous Membranes 601
A Contribution to the Radiological Examination of the Pericardium . 601
The Transmission of Experimental Syphilis to Man 602
Hypersensitiveness to Arsenic 602

SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D., AND T. TURNER THOMAS, M.D.

The Transplantation of the Hair-covered Skin 603
The Commandments of Modern Urinary Practice 603
A Contribution to Malignant Tumors of the Testicle, especially the Epitheliomatous 604
The Treatment of Dislocation of the Humerus with Fracture of the Head 605
Operation on Perforated Stomach and Duodenal Ulcers 605
Alcohol for the Prevention of Acute Cocaine Poisoning 606
Interparietomuscular Pyloropexy as a Method of Closing the Pylorus in Gastroptosis with Gastrectasia 606

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.

Clinical and Laboratory Salvarsan Relapses and their Remedy 607
The Dose and Methods of Application of Radio-active Substances in Internal Medicine 608
Therapeutic Pneumothorax as a Palliative Measure 608
The Röntgen Ray Treatment of Ringworm 609
Pneumothorax Treatment of Tuberculosis of Lungs 609
Eucalyptus Oil in Scarlet Fever and Measles 610
"Specific" Use of Salicylates in Acute Rheumatism 610

PEDIATRICS

UNDER THE CHARGE OF

LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.

The Meningeal Form of Poliomyelitis 611
Whooping Cough in the First Days of Life 612
"Tic" in Children 612
Pyuria in Infancy 613

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

The Treatment of Puerperal Sepsis at the Sloane Hospital for Women 614
Rupture of the Uterus 614

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.

Tuberculosis of the Cervix 617
The Role of Tuberculosis in the Production of Cystic Neoplasms . . 617
Cysts of the Cervix Uteri 618

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D., AND MARK W. RICHARDSON, M.D.

Experimental Beriberi 619
Perineal Abscess in a Typhoid Bacillus Carrier 620

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.

The Effect of Salvarsan on the Circulatory and Renal Systems . . . 621
Thrombosis in the Lymphatic Channels. 621
Palæopathology 622
Tubercle Bacilli in the Feces 622
The Bacteriology of Condensed Milk 623
Arterial Lesions in Rheumatic Fever 623
Anthracosis 624